PEDIATRIC CLINICS OF NORTH AMERICA

COPYRIGHT, 1954, BY W. B. SAUNDERS COMPANY

COPYRIGHT UNDER THE INTERNATIONAL COPYRIGHT UNION

All Rights Reserved. This book is protected by copyright.
No part of it may be duplicated or reproduced
without written permission from the publisher.

MADE IN U.S.A. PRESS OF W. B. SAUNDERS COMPANY, PHILADELPHIA

Library of Congress Catalog Card Number: 54-6097

CONTRIBUTORS

NOVEMBER ISSUE

ROBERT H. ALWAY, M.D., F.A.A.P. Professor and Head of Department of Pediatrics, University of Colorado Medical Center and Colorado General Hospital; Alternate Chief, Division of Pediatrics, Denver General Hospital; Director of Pediatrics, National Jewish Hospital; Pediatric Consultant, The Children's Hospital and Fitzsimmons Army Hospital, Denver.

JAY M. ARENA, M.D., F.A.A.P. Associate Professor of Pediatrics, Duke University School of Medicine; Associate Pediatrician, Duke Hospital; Visiting Pediatrician, Watts Hospital, Durham, N.C.

RUTH MORRIS BAKWIN, M.D., F.A.A.P. Associate Professor of Clinical Pediatrics, New York University Medical School; Consulting Director in Pediatrics, New York Infirmary; Associate Visiting Physician, Children's Medical Service, Bellevue Hospital, City of New York.

PAUL DONALD BRUNS, M.D. Associate Professor, University of Colorado Medical Center, Denver.

TAGUE CLEMENT CHISHOLM, M.D., F.A.C.S., F.A.A.P. Clinical Assistant Professor of Surgery, University of Minnesota Medical School; Attending Pediatric Surgeon, Minneapolis General Hospital, Minneapolis.

NORMAN W. CLEIN, M.D., F.A.C.A., F.A.A.P. Assistant Clinical Professor of Pediatrics, University of Washington School of Medicine; Chief of Pediatric Allergy Clinic, King County Hospital, Seattle.

JEAN CRUMP, M.D., F.A.A.P. Professor of Pediatrics, Woman's Medical School; Senior Active Staff, Hospital of the Woman's Medical College; Chief in Pediatrics, Woman's Hospital, Philadelphia.

SUSAN C. DEES, M.D., F.A.A.P. Associate Professor of Pediatrics and Allergy, Duke University Medical School and Duke University Hospital, Durham, N.C.

HARRY F. DIETRICH, M.D., F.A.A.P. Clinical Professor of Pediatrics, University of California Medical School; St. John's Hospital, Santa Monica Hospital, St. Vincent's Hospital, Good Samaritan Hospital, Cedars of Lebanon Hospital, Children's Hospital, Los Angeles; Hollywood Presbyterian Hospital, Beverly Hills Clinic.

JOSEPH H. FRIES, M.D., F.A.C.P., F.A.A.P. Chief of Allergy, Lutheran Hospital; Associate Attending Physician, Kings County Hospital; Allergist to Jewish Hospital of Brook-

lyn, Prospect Heights Hospital and Kingston Avenue Hospital for Contagious Disease, Brooklyn.

JEROME GLASER, M.D., F.A.A.P. Assistant Professor of Pediatrics, University of Rochester School of Medicine and Dentistry; Pediatrician-in-Chief, Genesee Hospital; Consulting Pediatrician, Rochester General and St. Mary's Hospitals, Rochester, N.Y.

PAUL H. HOLINGER, M.D., F.A.C.P., F.A.C.S. Professor of Broncho-Esophagology, University of Illinois College of Medicine; Attending Broncho-esophagologist, St. Luke's and Children's Memorial Hospital; Research and Educational Hospitals, University of Illinois College of Medicine; Consultant, City of Chicago Municipal Tuberculosis Sanitarium, Chicago and U.S. Naval Hospital, Great Lakes, Ill.

KENNETH CLAYTON JOHNSTON, M.D. Clinical Assistant Professor of Broncho-Esophagology, University of Illinois College of Medicine; Associate Attending Broncholologist, Children's Memorial Hospital; Attending Bronchoesophagologist, St. Luke's Hospital; Attending Bronchologist, Chicago State Tuberculosis Sanitarium, Chicago.

DOUGLAS EDWARD JOHNSTONE, M.D. Instructor in Pediatrics, University of Rochester School of Medicine and Dentistry; Pediatrician to the Pediatric Allergy Clinic, Strong Memorial Hospital; Assistant in Pediatrics, Strong Memorial Hospital and Genesee Hospital; Pediatric Allergist, Pediatric Allergy Clinic, Strong Memorial Hospital, Rochester, N.Y.

SAMUEL J. LEVIN, M.D., F.A.A.P. Assistant Professor of Pediatrics (Allergy), Wayne University College of Medicine; Director, Allergy Clinic, and Associate Pediatrician, Children's Hospital of Michigan; Senior Attending Allergist, Woman's Hospital; Assistant Pediatrician (Allergy), Harper Hospital; Associate Attending Internal Medicine (Allergy), Sinai Hospital, Detroit.

SAMUEL LIVINGSTON, M.D. Assistant Professor of Pediatrics, Johns Hopkins University School of Medicine; Physician-in-Charge, Johns Hopkins Hospital Epilepsy Clinic; Associate Attending Physician in Pediatrics and Assistant Physician in Medicine, Sinai Hospital, Baltimore, Md.

GEORGE B. LOGAN, M.D., M.S., F.A.A.P. Associate Professor of Pediatrics, Mayo Foundation, Graduate School, University of Minnesota; Consultant, Section of Pediatrics, Mayo Clinic, Rochester, Minn.

THOMAS C. McOSKER, M.D. Associate Neurosurgeon, Rhode Island Hospital; Visiting Surgeon, Charles V. Chapin Hospital, Providence, R.I.

ABE MATHESON, M.D., F.A.A.P. Licentiate, American Board of Pediatrics and American Board of Pediatric Allergy; Member, American Academy of Allergy; Attending Pediatrician, Michael Reese Hospital, Chicago.

HARRY L. MUELLER, M.D., F.A.A.P. Instructor in Pediatrics, Harvard Medical School; Visiting Physician, Department of Medicine, and Associate Allergist, Division of Allergy, Children's Medical Center, Boston.

ALEXANDER S. NADAS, M.D., F.A.A.P. Clinical Associate in Pediatrics, Harvard Medical School; Cardiologist, Children's Medical Center, Boston.

LLOYD S. NELSON, M.D., F.A.A.P. Clinical Instructor, University of Minnesota Department of Pediatrics; Chief of Pediatric Service, St. Barnabas' Hospital; Active Staff, Minneapolis General and Asbury Hospitals, Minneapolis.

JAMES OVERALL, M.D., F.A.A.P. Associate Professor of Clinical Pediatrics, in charge of Pediatric Allergic Clinic, Vanderbilt Medical School, Nashville, Tenn.

DONALD EVERETT PICKERING, M.D. Instructor, University of California Medical School;

Director, Pediatric Metabolic Laboratory, University of California Medical Center, San Francisco.

WILFRED PICKLES, M.D., F.A.C.S. Surgeon-in-Chief, Department of Neurosurgery, Rhode Island Hospital; Consulting Surgeon, Charles V. Chapin Hospital, Providence Lying-in Hospital, Miriam Hospital, Roger Williams General Hospital, Providence, R.I.

BRET RATNER, M.D., F.A.A.P. Professor of Clinical Pediatrics and Associate Professor of Immunology, New York Medical College, Flower and Fifth Avenue Hospitals; Director of Pediatrics and Allergy, Flower and Fifth Avenue Hospitals, City of New York.

FREDERIC SPEER, M.D., F.A.A.P. Associate in Pediatrics, University of Kansas; Director, Allergy Clinic, Children's Mercy Hospital, Kansas City, Mo.

BERNARD J. SPENCER, M.D. Attending Pediatric Surgeon, Minneapolis General Hospital, Minn.

ALBERT V. STOESSER, M.D. Clinical Professor and Director of Pediatric and Allergy Clinics, University of Minnesota Hospital; Active Member of Pediatric Staff and Consultant in Allergy, St. Barnabas Hospital, Minneapolis.

ROBERT W. WINTERS, M.D. University of California Medical Center; Bank of America-Giannini Foundation; Fellow in Pediatrics, University of California Hospital, San Francisco.

OSWALD S. WYATT, M.D., F.A.A.P. Clinical Professor of Surgery, University of Minnesota Medical School; Head, Pediatric Surgery, Minneapolis General Hospital, Minneapolis.

CONTENTS

SYMPOSIUM ON
ACCIDENTS AND EMERGENCIES

Page 757	**Robert H. Alway, M.D.**	*Foreword*
759	**Harry F. Dietrich, M.D.**	*Accident Prevention in Childhood Is Your Problem, Too*
771	**Jay M. Arena, M.D.**	*Poisoning in Infants and Children*
787	**Wilfred Pickles, M.D.** **Thomas C. McOsker, M.D.**	*Head Injuries in Children*
801	**Samuel Livingston, M. D.**	*Management of the Isolated Convulsion*
811	**George B. Logan, M.D.**	*Emergencies of the Respiratory Tract in Infants and Children*
827	**Paul H. Holinger, M.D.** **Kenneth C. Johnston, M.D.**	*Foreign Bodies in the Air and Food Passages*
845	**Paul D. Bruns, M.D.**	*Resuscitation of the Newborn*
859	**Alexander S. Nadas, M.D.**	*Cardiac Emergencies*
873	**Donald E. Pickering, M.D.** **Robert W. Winters, M.D.**	*Fluid and Electrolyte Management in Children*
901	**Robert H. Alway, M.D.**	*Management of Acute Phase of Thermal Burns in Children*
907	**Tague C. Chisholm, M.D.** **Bernard J. Spencer, M.D.** **Oswald S. Wyatt, M.D.**	*Intestinal Obstruction in Early Infancy*

SYMPOSIUM ON PEDIATRIC ALLERGY

919 **Jerome Glaser, M.D.** — *Foreword*

921 **Ruth Morris Bakwin, M.D.** — *Essentials of Psychosomatics in Allergic Children*

929 **A. Matheson, M.D.** — *Skin Tests and Their Value in Pediatric Allergy*

943 **Bret Ratner, M.D.** — *General Management of Allergic Children*

949 **Norman W. Clein, M.D.** — *Cow's Milk Allergy in Infants*

963 **Lloyd S. Nelson, M.D.**
Albert V. Stoesser, M.D. — *Local Treatment of Atopic Dermatitis*

969 **James C. Overall, M.D.** — *ACTH and Cortisone in the Treatment of Atopic Dermatitis*

975 **Samuel J. Levin, M.D.** — *Management of the Acute Asthmatic Attack in Childhood*

987 **Jean Crump, M.D.** — *Value of Vaccine Treatment in Allergic Respiratory Conditions*

995 **Joseph H. Fries, M.D.** — *Gastrointestinal Manifestations of Allergy in Children*

1007 **Douglas E. Johnstone, M.D.** — *The Allergic Celiac Syndrome*

1017 **Susan C. Dees, M.D.** — *Neurologic Allergy in Childhood*

1029 **Frederic Speer, M.D.** — *The Allergic Tension-Fatigue Syndrome*

1039 **Harry L. Mueller, M.D.** — *Dosage in the Treatment of Pollinosis*

1047 — *Index of Authors*

1049 — *Index to Volume 1 (1954)*

FOREWORD

ROBERT H. ALWAY, M.D.

Pediatric accidents are not the result of the negligence or malfeasance of children, but of adults. "Accident proneness" may sometimes be shown to be a characteristic of some children, but too often it appears to be the parents who invite accidents by leaving attractive hazards at hand. As either a parent or a physician we cannot honestly say that childhood accidents happen without expectation or foresight. Accordingly, the paper on Accident Prevention deserves priority and major emphasis. Other papers dealing with accidents have been included, however, to cover our lack of foresight. Nonaccident emergencies being no less harrowing, papers on Convulsions, Neonatal Resuscitation and Respiratory and Cardiac Emergencies have been included.

Since the victims of pediatric accidents and other emergencies include not only the children, but parents and physicians as well, this Symposium was organized with the hope of helping all three. The selection of subjects was based both on incidence and the need for up-to-date advice on their management. The Consulting Editor has been most fortunate in obtaining the aid of experts whose presentations of their particular subjects have seemed especially felicitous.

ACCIDENT PREVENTION IN CHILDHOOD IS YOUR PROBLEM, TOO

HARRY F. DIETRICH, M.D.

There is a considerable inclination to brush off discussions of accident prevention in childhood with one of two lethal attitudes. Both "I've heard all about that" and "You can't do anything about such a complex problem" are equally devoid of a conscientious physician's usual attitude towards a difficult problem.

No problem can be solved unless it is defined; some factual material is necessary to illuminate that definition and, I believe, to suggest a solution. Here, then, are some facts about accidents in childhood:

1. Twelve thousand to 13,000 children are killed by accident in the United States each year.[1]

2. Forty thousand to 50,000 is a conservative estimate of the number of children permanently injured each year by accident.[4]

3. One million is certainly the minimal number who seek medical care each year because of accident.[5]

This is certainly a big enough problem to warrant our attention. One extremely important additional fact provides a valuable clue as to where first to direct that attention. Approximately half of all fatal childhood accidents occur in the first third of childhood! Sixty-five hundred children under five years of age are killed by accident in the United States each year. Suppose, as a starter, we try to prevent serious accidents in children in the preschool age group; in this admitted simplification of the accident problem we have deleted two thirds of the one year age groups and their variable problems, while retaining one half of the actual problem of accidental death and crippling.

If we are looking for a starting point, this is it. Let us take as our problem the prevention of lethal and crippling accidents in children

From the Division of Pediatrics, The Beverly Hills Clinic, and the Department of Pediatrics, University of California Medical School, Los Angeles.

from birth to five years of age. This doesn't sound, and isn't, as formidable as "accident prevention in childhood." Before attempting to suggest a practical theory of accident prevention, examine, even if casually, the most common types of lethal accidents in the age group under consideration (Fig. 1). No, there really are not too many things to

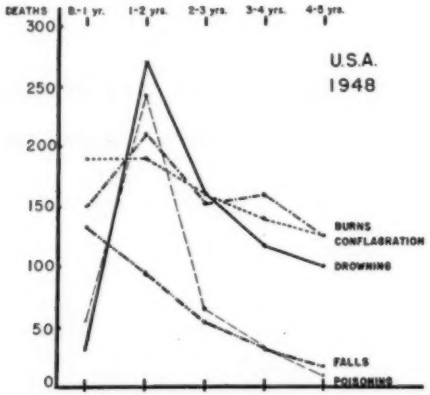

Fig. 1. Principal causes of accidental deaths.

think of. Figure 1 not only indicates the most common causes of accidental death for each one year age group, but also dramatically emphasizes the most dangerous age.

Automotive deaths are not included in Figure 1, but are worthy of separate examination and thought (Table 1). Unless we wish to teach

TABLE 1. *Motor Vehicle Accident Deaths, Birth through 5 Years, United States, 1952*

TYPE	NUMBER	FAULT
Pedestrian	900	Child + adult
Collision with vehicle	650	Adult
Overturning, and so on	430	Adult
Collision with object	30	Adult
Collision with railroad	40	Adult
Total	2050	55% plus adult

the preschool child not to ride in automobiles with adults, the major part of the prevention of vehicular deaths in the birth to five year age group is not a juvenile problem. What can we do to prevent the five main causes of accidental death and crippling in the preschool child? I believe that we must agree that the young infant, defenseless and inexperienced as he is, must be given 100 per cent protection from burning, drowning, poisoning, crushing and falling. That should make acci-

dent prevention in the first year of life quite simple, but it is not so simple as to permit us to ignore it. Passing over some important intervening years, consider the child, when at five years of age he starts to school or goes to play with a neighborhood friend. He has access to every accident hazard. Will he dash into the road, run into the pond, touch a match to the pile of rubbish in the barn, drink a plant spray, insert a nail or bobby pin into an electrical outlet, or turn on and toy with the power machinery? If he won't do these suicidal acts, why won't he? Was it a slogan written in icing on his fifth birthday cake that suddenly gave him safe behavior? It must be apparent that the safety of the five year old depends primarily on what he knows, and it must be equally obvious that he cannot acquire that education by edict on a chosen day. Like all education, it is the fruit of step-by-step learning.

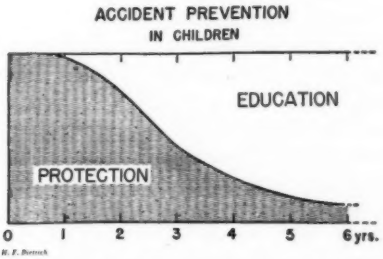

Fig. 2. The reciprocal relationship between protection and education related to age, as indicated in the theory of accident prevention.

Like all behavior, it is the result of hero (parent) example, supervised experience and, to a much lesser degree, orthodox instruction.

What have we said so far? Accident prevention under one year of age requires 100 per cent protection; by five years of age we must rely principally on what the child knows. The years from one to five, therefore, must be occupied by diminishing protection and by imaginatively, bravely, increasing educational experience. There always remains an irreducible segment of protection at each age against the too serious or too subtle accident hazards. That sounds like theory—it is, and it can be diagrammed as in Figure 2.

In order to transfer this theory from a line drawing, to accident prevention in the home, three tools are indispensable, and adequate. Forethought, time and discipline are requisite. Forethought demands that at any age the child's interests and abilities be anticipated; considering those curiosities and capabilities, a prediction of the child's probable conduct should indicate what protective measures will be necessary, and in what areas of activity instruction will keep him out of serious accident. Of course such an attack on accident prevention takes time. It

takes time to sterilize bottles, to brush teeth, to wash ears, to polish shoes, to iron dresses, to teach nursery rhymes, to worry about normally small appetites, to choose and use a toilet seat, to talk to relatives about the baby's first step, to get everything just right for snapshots, to change diapers, to listen to the woman at the market explain how to prevent and treat colds, to have the shoe salesman explain the foot problems of children, to measure fever by tenths of degrees, and to discuss with a neighbor which brand of vitamin B_{12} induces the most growth, and which one of B_1 the most appetite. All these things and accident prevention take time. On what would you advise parents to spend their time?

Forethought, Time and Discipline

Discipline must serve where reason cannot. What other means can be used to keep the sixteenth months old child away from the kitchen stove, and the three year old youngster out of the street or stream? What is disciplinary control? Basically, it is the child's knowledge, born of experience, that his own interests are best served by following the course directed by the obviously loving parent. Deviation from that course might reasonably be expected to result in parental disapproval, a stern word, deprivation of a privilege (in the instance of the stove problem, banishment from the kitchen), or gluteal erythema. In any event, discipline should be mild, logical, consistent, related to the offense if possible and understandable by the child. Every child desperately needs to know that his parents will not permit him to do any truly injurious or self-embarrassing act; he will repeatedly test his parents to reassure himself of the existence of this disciplinary halter. Under such circumstances there can be no more reasonable and acceptable field for the exercise of discipline than in the area of accident prevention. If, during the first three years of life, discipline concerns itself only with the things that threaten the child's safety, it will be quantitatively right in amount, literally vital in its results, and happily acceptable by the child. So far it doesn't sound too impossible, does it? Parenthetically, accident prevention in childhood will never be easy, and it will never be instituted early enough, unless it is done by the parents in the home. It is up to the medical and allied professions, aided perhaps by the propaganda impact of militant lay organizations, to convince parents of (1) the importance of the accident problem, (2) the triviality of most parents' worries about their children, (3) the feasibility and vital economy of teaching children safe behavior.

One of the reasons why the problem of accident prevention in childhood has appeared to be insurmountable has been the obvious inability of parents (or doctors) to anticipate, at one instant, all accident hazards

for all children, of all ages, of either sex, living in any community. Such a kaleidoscopic conception is unnecessary and overwhelmingly confusing. There should be adopted, instead, a logical and justifiable simplification. For any single child, of given sex, of specified age, living in a stated family and community situation, consider:

1. What are its abilities, interests and opportunities?
   a. To what hazards is it thereby exposed?
      (1) What protection is needed?
      (2) What education is practical?

Viewed in this segmental manner, accident prevention presents as a practically assailable problem—challenging but soluble, and infinitely rewarding. And now to do exactly the thing we should not do for the individual child, consider briefly (and with many omissions) a few of the protective and educational measures that must be taken for virtually all children during the first two years of life.

THE INFANT

During the first year we must depend on protection. The infant must not be left where, when it rolls over or stands for the first time, it can fall and suffer a serious injury. He should not be restrained by sleeping garments that may choke him. He should not (even for the "minute" necessary to answer the telephone or door bell) be left where he can drown or scald himself. He should not be left under such circumstances that a household fire can consume or asphyxiate him. He should not be given objects or toys on which he can choke. Protect him from poisoning. Don't paint his furniture or toys with lead base paint.

Give medication only on the advice of a doctor. Provide him early (three to four months of age) with a place, such as a play-pen, where he can safely be left without supervision. When he is ready, at five or six months of age, for a high chair or a seat at a table, be certain that it is placed where hot substances cannot be spilled on him and where he cannot reach potentially harmful objects and pull them on himself. Remember that no child has cracked his skull or addled his brain by not having a bowel movement, but many have done so trying to produce one while sitting on a juvenile toilet seat.

There is scant opportunity for actual safety education under one year of age, but there is a logical place for the introduction of the first attempts at disciplinary control at nine to ten months of age. At this time the infant actively resists, and increasingly effectively fights, being put on his back while his diapers are changed. Yet this sartorial custom of our culture must be repeated many times daily for many months to come, and the increasingly successful struggles of the infant constitute a real threat to his safety. Because it is the contention of this writer that

(1) discipline is as necessary to a child's sense of security as it is to his safety, and that (2) during the first three years of life mild, consistent, logical and understandable discipline should concern itself only with the things that threaten a child's safety, it would seem that the daily pants pandemonium, which constitutes a repeated threat to the safety of the infant, demands the introduction, at this tender age, of discipline. If the necessary disciplinary control can be achieved by a firm word, that's wonderful, and adequate, and surprising; if it should require a few swats on the area being serviced, this will be tolerated by the beloved infant, even if it cannot be by many parents and some psychiatrists.

THE TODDLER

Because of the frightening and tragic rise in the incidence of accidental death in the one to two year age group, let us direct our attention to this critical period. By way of providing protection for the infant, it is probably wise to warn parents that only now, as the infant achieves ambulatory mobility, is the play-pen reaching its maximal usefulness. A child can be given a supervised period of greater physical freedom without completely discarding the play-pen or wire enclosure in the yard. Though I daily hear of one year old infants who "won't stay in a play-pen," I have never seen one who could climb out under his own power. The increased physical prowess and normal curiosity of the one year older demand now, more than ever before, that his mother have a place where she can safely leave him without minute-to-minute supervision. There is no valid psychologic reason why the play-pen, policed and gated room or similar enclosure should not be used until he is eighteen to twenty months of age.

Since the mortality and morbidity figures clearly demonstrate the need for increased protection against lethal hazards in this age group, it is not too early to use some simple educational devices. One important educational technique is to let the child learn from his minor accidental injuries. This implies the use of two important procedures: (1) Explaining objectively why the injury occurred or, even better, predicting why it is likely to occur. "It is hot, and it will burn your finger if you touch it." (2) Refraining from rewarding minor injuries with emotional or saccharine poultices.

Parents are often advised: "Leave the house just the way you want it—the child has to learn to live in it." This is a vicious bit of instruction, and when it is adopted, the child is at first confused, then annoyed by, and finally inured to, the endless succession of equally emphatic "Don'ts" about the cigarette box, the electrical outlets, the bric-a-brac the letter opener, the ink bottle and the stove. During the period of compulsive exploration the child's world should be simplified as much

as possible; unnecessary temptation should be removed from reach, if not from view. In the age period from two to three years he will be much more interested in testing people than objects, and then things can slowly be returned to their accustomed places.

Consider briefly, and for your own elaboration, the measures necessary to prevent the most serious types of injuries in the one to two year old child.

Burns

Protection demands that these toddlers not be allowed near the stove, whether or not it is in use. They must be denied access to open flames and radiant coils. They should not be permitted to contact matches or table lighters. They should not be left in circumstances in which unexpected conflagration could consume them. Unused and accessible electrical outlets should have plastic plugs; locking safety outlets are good insurance if necessary electrical cords are in good repair. These relatively helpless youngsters should not be permitted to play or sit where hot substances can be spilled by or on them. The makeshift steam kettle should be used only when the disease being treated is more serious than the potential burn. Clothing and playthings should not be made of highly inflammable materials.[3] Solar radiation should be accorded adequate respect.

Educational opportunities are relatively few, but vitally important. The eighteen months old toddler must gain the concept of "hot." He can most cogently do so if, when he first reaches for a hot object such as a lighted cigarette, one parent will calmly say, "That's hot, it will burn your fingers." Notice that the infant is not forbidden to touch the cigarette; he is honestly warned of the true consequences of his (inevitable) act. From such a simple experience he learns two things: (1) the concept of "hot," and (2) that the parent tried to warn him of the unpleasant results of his intended action. The parent thereby gains stature as a prophet and protector.

Drowning[4]

The toddler must not have unsupervised access to any body of fluid larger than a kettle full. The few inches of water in a bath tub, 6-inch-deep ponds and 100-foot-deep quarries all combine to make the peak incidence of drowning in the preschool child occur in the one to two year age group. Obviously more protection is needed. The minute necessary to answer the telephone or door bell, or shut off the oven, has too often proved long enough to drown the unwary toddler.

Is there a place for education of the toddler against drowning? Un-

fortunately the first eighteen months of an infant's life are spent giving him daily lessons to convince him that he is unsinkable. In the bath, with loving intent and vicious effect, he daily hears and feels, "Watch baby swim! Isn't that water wonderful!" And in these same formative months only the alleged virtues of water are emphasized. "Drink it, and you'll grow big or get well"; "Let me use it on your face and you'll be clean (and therefore good, and so I'll love you)"; "Put your bowel movement in it and you'll be the family hero." Never a thought or word about the unpleasant effects of water in the respiratory passages. Yes, adequate education, even at this age, might well provide controlled experience with the unpleasantness of aspirated water. Remember, we are trying *not* to gamble with big stakes. Then, perhaps, parents would not be so proud that "he has absolutely no fear of (respect for) water," or so tragically surprised when the twenty months old infant blithely steps into 10 feet of it.

Falls

The exploring toddler must be protected from falls from heights, onto injurious surfaces, or with dangerous objects in his hands. Prudent protection would seem to require that window screens be secured and stairways be guarded with gates. In a car he should ride standing on the front seat behind the right shoulder of the driver, or standing against the dash board or against the back of the front seat. It should be borne in mind that all conventional car doors can be opened from the inside even when they are "locked." If the youngster is permitted to climb on a chair or bed or box, certainly the potential landing areas should be free of extraneous objects, and he should not be permitted to have sharp objects in his hand. His high chair should be placed where he cannot overturn it by pushing against a wall, and he should be securely strapped into it. He should be chaperoned while on his toilet seat for three sound reasons: (1) His stay on it should be so short (two to three minutes) that it isn't worth leaving him him alone; (2) so that he can be taken off immediately if he doesn't want to stay on it, and (3) in order that he can be mildly praised and promptly taken off if he and chance produce some results.

Education to prevent serious falls at this age has limited but well defined value. Certainly every youngster must learn that gravity is always tugging at the seat of his pants, and so again it is important that the parents objectively point out the cause of the minor tumble, rather than solace the pain of it with a reward. Even at this age the child can learn that he will be permitted climbing adventures within his capabilities, provided he observes the clear landing field and unencumbered hands restrictions.

Poisoning

Perhaps nowhere is adequate protection so important, for from the moment of birth parents have taught the child the virtue of putting everything into his mouth. Therefore it is criminal to leave any toxic substance where the evergrowing reach and insatiable curiosity of the normal child will transfer it to his mouth. Here we physicians have one inescapable and personal responsibility. We have encouraged the drug houses into taking scores of potentially deadly poisons and disguising them to look and taste like candy. We endorse by prescription these disguised poisons, and then fail to warn parents of their dangers in overdosage. And then we are righteously annoyed when "parents leave them where the children can get them." These poisons are far more subtly and ingeniously prepared than are the ordinary poisonous grains which successfully exterminate mature and wise rodents.

So when we speak of education against poisoning, perhaps we physicians had better take the first lesson. But we can begin to teach the child even at eighteen months of age that not every substance is pleasantly imbibable. A parent might place a small glass of vinegar where a child can reach it and, after warning him that "It doesn't taste good," passively permit him to taste it. Similar experiences with a paste, such as hot English mustard and a powder such as alum or bicarbonate of soda, will effectively teach the youngster that not all liquids, pastes and powders taste as good as his highly touted foods do. With such education the child will soon bring strange substances to the parent to inquire, in effect, "Does it taste good?"

If it appears that our preoccupation with the first two years of life has been too great, refer to Figure 1. Two facts are noteworthy: The high incidence of fatal accidents in the one to two year age group imposes the necessity for concern with increased protection. Further, and more stimulating perhaps, the declining incidence of those serious accidents from two to five years of age suggests that, even without outside intervention, children begin to learn safer behavior. This tendency offers fertile soil on which parents can profitably expend additional educational effort. These educational projects, as was earlier suggested, should be determined by the interest and abilities of the child.

Accident Proneness

Accident proneness is a fairly well established, though occasionally questioned[8] concept in the adult field. The most widely held precepts cannot be directly transferred to the childhood area of accident determinants.

In studying minor accidents Fuller[9] has shown that the accident-prone nursery school child is an attractive, rather to-be-admired young-

ster. There are individual cases reported of emotionally unstable or disturbed children who had a tendency to accidents. In an intensely studied small pilot group Langford and his co-workers[10] found that juvenile accident repeaters come from families in which there was an astounding incidence of serious accidents in collateral members of the family. It is my personal belief that in the instance of the preschool accident repeater, close scrutiny and instruction of those adults responsible for his care might be most profitable. At present we can only say that the accident-prone young child has not been identified as a psychologic entity, nor has he been distinctly isolated from the "child-accident-prone parent."

SUMMARY

It must now be apparent that the problem of juvenile accident prevention is unique in medicine. We are faced with a condition which embraces a tremendous morbidity and mortality. We have an effective immunizing vaccine in the form of protection and education related to age. But, and this is how the problem of accident prevention differs from all other immunization procedures, the vaccine must be administered in the home and by the parents. Mass indoctrination of parents may be feasible, but the inoculation of the child is an individual, personal responsibility of the parent. Armstrong and Cole[2] have concisely presented a practical plan of organization for a community child safety program.

The current needs in the field of accident prevention in childhood are many and varied:

1. Using the ideas and materials available, we need to impress parents with the importance and practicability of accident prevention.
2. More information on the cause of accidents is needed.
3. Better parent education materials are necessary.
4. Critical studies of parent and community education techniques are imperative.
5. Every physician must assume responsibility for counseling at least his own patients; many can take community leadership, and some will want to add to our basic knowledge and so improve our vaccine and the ways of administering it.

What are *you* doing about it?

REFERENCES

1. Accident Facts. Chicago, National Safety Council, 1953.
2. Armstrong, D. B., and Cole, W. G.: Can Child Accidents Be Prevented in Your Community? Am. J. Pub. Health, 39:585, 1949.

3. Colebrook, L.: The Prevention of Burning Accidents in England and America. Bull. New York Acad. Med., 27:425, 1951.
4. Dietrich, H. F.: Accidents, Childhood's Greatest Physical Threat, Are Preventable. J.A.M.A., 144:1175, 1950.
5. Dietrich, H. F.: The Clinical Application of the Theory of Accident Prevention. Am. J. Pub. Health, 42:849, 1952.
6. Dietrich, H. F.: The Prevention of Drowning. GP, 7:61, 1953.
7. Dietrich, H. F.: Teach My Children—They Will Prevent Your Fires. Quart. Nat. Fire Protect. A., 47:9, 1953.
8. Editorial: Accident Proneness. South African M.J., 27:321, 1953.
9. Fuller, Elizabeth M.: Injury-Prone Children. Am. J. Orthopsychiat., 18:708, 1948.
10. Langford, W. S., Gilder, R., Jr., Wilking, V. N., Genn, M. M., and Sherrill, H. H.: Pilot Study of Childhood Accidents. Pediatrics, 11:405, 1953.

133 South Lasky Drive
Beverly Hills, Calif.

POISONING IN INFANTS AND CHILDREN

JAY M. ARENA, M.D.

More than 1000 American children die annually from the accidental ingestion of poison. The actual number is probably much greater, since many fatalities from poisoning are not recognized as such. The mortality is only a part of the picture, however. Many children who survive the ingestion of poison are left with permanent disabilities—for example, esophageal strictures following caustic alkali (lye) poisoning, and the hepatic or renal damage caused by many other toxic agents. Practically all these deaths and disabilities are caused by the ingestion of poisons contained in household agents.

In the absence of a definite history of the ingestion of, or contact with, a known poisonous substance, the symptoms and signs presented by a case seen in emergency may not suggest a diagnosis of poisoning. Nevertheless, the possibility of poisoning should always be considered in a puzzling situation when differential diagnosis presents a difficult problem.

Ingestion of poisons and usually also inhalation or absorption through the skin will generally cause gastrointestinal disturbances, including anorexia, abdominal pain, nausea, vomiting and diarrhea. Such symptoms are not diagnostic, however, since they occur in many disorders of childhood.

Respiratory and circulatory symptoms are also prominent in most cases of acute poisoning. This diagnosis should be considered whenever one is confronted by unexplained cyanosis, shock, collapse, sudden loss of consciousness, or convulsions. Again, these symptoms are not pathognomonic, since they may occur as a result of many severe conditions.

From the Department of Pediatrics, Duke University School of Medicine and Duke Hospital, Durham, N. C.

In spite of the obstacles imposed by lack of distinguishing symptoms and the difficulty or impossibility of obtaining a history from patients who are too young, too ill or too frightened to be of assistance, a high index of suspicion and a little ingenious detective work will frequently establish the correct diagnosis and lead to identification of the poison.

Fig. 3. Principal sources of accidental poisoning of children.

Knowledge of the sources, actions and therapy of every known poison is desirable. Command of the general principles of management, however, is even more desirable, for too often the next poison encountered will be due to a new or not readily identifiable substance.

Clues can sometimes be obtained from relatives, friends or bystanders. In addition, the vomitus, the material obtained by gastric lavage, and the first urine specimen may yield decisive evidence. Also, the characteristic odors of many poisons may be detected on the patient's breath.

Laboratory studies of the blood unfortunately require time even if facilities for them are available. When it is possible, spectroscopic

examination of the blood will establish the presence or absence of methemoglobin, sulfhemoglobin and carboxyhemoglobin. Also lead, bromine, thymol and many other toxic substances can be detected by use of a photoelectric colorimeter. X-ray studies of the bone are, of course, valuable in lead and bismuth poisoning.

CAUSTIC ALKALI (LYE) POISONING

A type of poisoning, seen frequently in certain sections of the South, from a household agent is caustic alkali poisoning from the ingestion of lye. Since the opening of Duke Hospital twenty-four years ago, over 250 children have been treated for stenosis of the esophagus from the ingestion of lye. Commercial lye preparations contain 95 per cent sodium hydroxide; cleansing solutions, washing powders and drainpipe cleansing agents contain 8 to 50 per cent of caustic alkali. Lye is still commonly used by poor people in the home manufacture of soap. The availability and widespread use of these materials account for the frequency of lye poisoning, especially in small children, despite the publicity which has been given it.

If the patient is seen immediately after the ingestion of the alkali, an attempt should be made to neutralize the corrosive with a weak acid such as dilute vinegar, lemon juice or orange juice. Gastric lavage is not indicated, since the alkali is neutralized in the stomach by hydrochloric acid; furthermore, it is doubtful whether much of the alkali reaches the stomach, since the first swallow causes severe pain, and very little is taken. The oral cavity should be examined carefully for damage to the uvula, soft palate or other parts of the posterior portion; such damage is usually an indication that some alkali has been swallowed and that erosion of the esophageal mucosa has probably occurred.

Esophagoscopic examination and/or barium swallow studies at this time are often useless. It is impossible to pick up in every instance the small areas of esophageal inflammation which eventually lead to stenosis in this early stage.

The patient should be given a sedative if he is restless, and the diet should consist of fluids and soft, nonirritating foods. If erosion of the esophageal mucosa is suspected, a soft rubber, eyeless catheter, filled with mercury or small lead shot, should be passed into the stomach at intervals to help prevent the formation of a stricture. The dilatations are usually begun on the fourth day after the ingestion of the alkali and are repeated daily for two weeks, during which time the size of the catheter is gradually increased until a number 32 or 34 catheter is passed with ease. Dilatations are then done at less frequent intervals, but should be continued for at least a year.

If a patient is seen several weeks after the ingestion of the alkali

and presents the symptoms of partial esophageal obstruction, one should not pass catheters blindly, but should do barium studies and esophagoscopy to determine the nature and extent of the esophageal damage. Peroral dilatations through the esophagoscope may be performed if there is a single strictured area which is not severe, but gastrostomy and retrograde dilatations are safer if multiple or very narrow strictures are found. Surgical procedures recently devised to correct esophageal strictures are being used more often.

KEROSENE (GASOLINE, BENZINE, NAPHTHA)

A common type of childhood poisoning is that due to kerosene, which is sometimes left carelessly about the house in a soft-drink bottle, and thirsty toddlers sometimes sample the liquid. When the substance has been ingested, early symptoms are burning pain in the mouth, esophagus and stomach, followed by headache, nausea and vomiting. Poisoning may cause acute toxemia with depression, pneumonia which may be severe, and at times degenerative changes in the liver, kidneys, lungs and heart. Emetics and gastric lavage are contraindicated. Thirty to 60 cc. of olive oil or mineral oil should be left in the stomach. Coramine and/or caffeine are valuable stimulants to combat depression. Antibiotics should be started early. Pulmonary edema can be treated with hypertonic glucose solution (50 per cent) and oxygen. Adequate fluids are essential, and blood transfusions may be indicated.

SODIUM FLUORIDE POISONING

Sodium fluoride poisoning resulting from the ingestion of roach powder is a lethal type of poisoning; the ingestion of any appreciable amount of this substance causes death within eight hours if prompt therapy is not given. The symptoms usually include severe hematemesis, abdominal cramps, weakness, shallow respirations and eventual respiratory failure. Hematuria is not often mentioned, but severe damage to the tubules and glomeruli of the kidneys has been reported. Treatment consists in immediate lavage of the stomach with any soluble calcium salt (chloride or lactate, for example) to change the soluble sodium fluoride to the insoluble and innocuous form of calcium fluoride. Calcium should also be given intravenously and intramuscularly. Supportive treatment should be carried out as necessary.

CASE REPORT. A 1 year old boy with a history of hematemesis for several hours was admitted to Duke Hospital. At noon on the day of admission his mother had noted that he was irritable, but he ate his lunch. Two hours later he vomited a small amount of blood. The hematemesis continued in progressively larger amounts. Five hours later (4 hours prior to admission) the parents noted that the child had gross hematuria and a yellow tint to his skin and that he was restless.

On admission the infant was drowsy, but responded well to stimuli. The urine in the diaper was grossly bloody. The skin was markedly icteric, but the scleras were clear. The urine contained albumin and many red blood cells in a centrifuged specimen; the benzidine test was positive. The blood count showed 28,000 white blood cells. The blood nonprotein nitrogen was 44 mg. per 100 ml. The results of other examinations were negative.

On close questioning the mother stated that the child had the habit of putting everything into his mouth. She denied poisoning, but stated that they had moved into a new home that very morning and that "anything could have happened."

On the suspicion that the patient had swallowed roach poison (sodium fluoride) his stomach was lavaged, and 30 cc. of calcium gluconate (10 per cent) were left in the stomach. Five cubic centimeters of 10 per cent calcium gluconate were given intravenously and 5 cc. intramuscularly. A transfusion of 180 ml. of whole blood also was given on the day of admission, and repeated the following morning. The parents at this time returned with samples of roach powder that had been scattered all over the house by the departing tenants. The patient was placed on a high protein and high carbohydrate diet and was given sodium bicarbonate and ascorbic acid. By the second hospital day the child was eating well and did not appear ill, although the albuminuria and hematuria persisted for 7 days. He was discharged on the ninth hospital day in good condition; his blood nonprotein nitrogen at that time was 34 mg. per 100 ml.

BARBITURATE INTOXICATION

The widespread use of sedatives by the general population has led to a marked increase of barbiturate intoxication in children. Practically every family medicine chest has been converted into a miniature barbiturate warehouse. The output of this drug has been growing so rapidly that in 1953 over a million pounds were produced in this country. Symptoms of acute poisoning are referable largely to the nervous and cardiovascular systems. Excitement and hallucinations may precede the depression. Respiration is soon affected. The resulting anoxia may cause capillary dilatation and permeability resulting in shock. The activity of the reflexes is inversely related to the intensity of the depression. The pupils usually react to light and may be dilated or constricted. Blood pressure falls rather late. Urination may be decreased or suppressed. The temperature falls, and the skin is cold, moist and cyanotic.

The *diagnosis* is usually made from the history and physical examination. Differentiation from poisoning caused by other central nervous system depressants or from coma due to other causes may be difficult. Identification of the drug in the gastric content or urine is often necessary.

The *prognosis* is dependent upon the amount and type of barbiturate ingested and on the efficacy and promptness of therapy. If the patient survives the first twenty-four to thirty-five hours, the chances of recovery are usually favorable. Death may occur as a result of paralysis of the respiratory center.

Treatment consists in gastric lavage in the early stages, but is con-

traindicated in comatose patients because of the danger of aspiration pneumonia. Glucose and saline intravenously and, if coma persists for several days, intravenous amino acids and water-soluble vitamins are administered. Oxygen is best given by endotracheal catheter. Antibiotics are indicated if the temperature becomes elevated. The use of low sodium human serum albumin to decrease cerebral edema has been recently found to be effective.

SALICYLATE INTOXICATION

Since the advent of candy aspirin, poisoning from this drug has become common and most serious throughout the nation. Dubow and Solomon[11] emphasized that the dosage of salicylates in acute rheumatic fever may be within the toxic range. Skin absorption of salicylic acid from an ointment has been known to cause death. The symptoms are (1) hyperpnea in all cases. This may be mild at first and may be overlooked, particularly in patients with cardiac involvement, in which the hyperpnea may be thought to be "cardiac dyspnea." (2) Apathy and lassitude may be striking. (3) Anorexia. Other signs are tinnitus, dizziness, irritability, stupor, high fever, convulsions, abdominal pain, epistaxis and other hemorrhagic manifestations and dehydration.

Treatment in the acute poisoning is immediate gastric lavage. Although the patient is hyperventilating, it should be kept in mind that the salicylic compound acts directly on the respiratory center, causing hyperpnea. The low carbon dioxide content values may be due to the blowing off of carbon dioxide, and the *p*H actually may be rising, and indiscriminate use of alkali at this time may push a harmless and transitory alkalosis to dangerous levels. Fluids alone and glucose intravenously to increase renal excretion are all that is necessary at this time. Later, owing to inanition, anorexia or dehydration, a true metabolic acidosis develops, at which time both the carbon dioxide content and *p*H values are low, and alkali therapy is then definitely indicated.

LEAD POISONING

Lead poisoning in children, though perhaps not as common as in the past, still occurs frequently enough that one should be alert for the symptoms whenever they appear.

Lead poisoning can be caused by ingestion, inhalation or absorption of lead from the skin (rarely seen in children). Poisoning by inhalation of lead from burning battery casings which contained lead sulfate and peroxide was first discovered by an observant intern (Dr. Mirion Bailey) at the Harriet Lane Home in 1932. The symptoms of lead

intoxication, whether from ingested or inhaled lead, are similar. The symptoms are more severe, however, when lead is inhaled, since lead is absorbed more rapidly and completely from the respiratory tract.

The gastrointestinal *symptoms* are vomiting, anorexia and constipation. Anemia due to destruction of the red blood cells may be moderate or severe; basophilic stippling is practically always present. The deposition of lead sulfide on the gum margins results in the lead lines seen in children after the teeth have erupted. Meningo-encephalitis is suspected when there are mental confusion, convulsions and projectile vomiting. Papilledema or optic atrophy may be discovered at this time. This is a severe complication, and the mortality rate in such cases is high (35 per cent). Neuritis is rare. Roentgenograms of the long bones are diagnostic in children, for they will show a zone of increased density at the ends of the bones beneath the epiphysial line.

After the source of lead has been removed from the child's environment, *treatment* consists in the administration of sodium citrate, 0.3 gm. every four hours (citrate ions combine with lead to form an insoluble and harmless complex which is slowly excreted), large doses of ascorbic acid, a diet rich in calcium, and calcium gluconate by mouth. Barbiturates will be necessary to control convulsions, if present. Calcium disodium versenate is a new drug which shows promise in the treatment of lead poisoning.

CASE REPORT. A 7 year old white boy was admitted to Duke Hospital in a moribund condition. He had had convulsions, generalized weakness, anorexia and constipation for 2 weeks. He expired before a complete examination could be made. However, marked papilledema was observed, and it was thought that he had had a brain tumor or tuberculous meningitis. No autopsy was permitted.

Five days later his 5 year old brother was admitted with similar complaints. This child was irritable and had severe generalized weakness. He also had marked papilledema. Lead poisoning was suspected, and on further questioning the source of lead was discovered to be from the burning of battery casings in the home. On closer examination of the child a lead line was seen at the gum margins, and roentgenograms of the long bones were typical of lead poisoning. The cerebrospinal fluid findings were consistent with the diagnosis of lead encephalitis. The child was treated vigorously and responded well.

ATROPINE, BELLADONNA AND STRAMONIUM

Stramonium is found in jimson-weed (thorn apple, stinkweed) and certain other plants. All parts of these plants are poisonous, but the seeds are especially toxic, since they contain atropine, scopolamine and hyoscyamine. Atropine eye drops and belladonna preparations occasionally cause poisoning in children.

The first *symptoms* of acute intoxication are burning and dryness of the mouth, intense thirst and visual disturbances. The pupils are widely dilated, do not react to light, and show failure of accommoda-

tion. Weakness, giddiness, a staggering gait, mental confusion, excitement and delirium ensue.

Withdrawal of the drug may be the only *therapy* necessary. In severe cases lavage the stomach with 4 per cent tannic acid solution; then give magnesium sulfate. Small doses of pilocarpine are useful. A quiet, dark room is essential, and sedatives should be given to control convulsions and motor activity. Large doses of sedatives can be dangerous. In later stages of intoxication, depression may occur, and stimulants are required. Artificial respiration, oxygen and carbon dioxide therapy may be necessary.

CASE REPORTS. A 3 year old white male child was admitted to Duke Hospital with a 5 hour history of staggering, confusion, inability to see well, dilated pupils and a flushed face. No atropine-like drugs were in the home, but the child had been noticed to be playing with a jimson-weed 8 hours previously. He had not eaten, urinated or defecated during the past 10 hours. The physical examination revealed a well nourished and developed child who was confused and staggering. The face was flushed, and the pupils were maximally dilated. The remainder of the physical examination revealed the pulse to be 130, the temperature was normal, and there was an ataxic gait with normal reflexes. The laboratory findings on the blood and urine were within normal limits.

A tap water enema was given upon admission, and the child was put on no medication, with observation of vital signs. There was an increase in excitability and hyperactivity during the first 7 hours after admisson, and after this a progressive decrease. There were no signs of respiratory depression. He was discharged 18 hours after admission, at which time he was rational and well coordinated, and, although the pupils were still markedly dilated, he showed no disturbance in vision. The pupils remained dilated to some extent for 2 days after discharge. Re-examination 10 days later revealed no abnormality.

The brother of the previous patient, a 21 month old white male, was admitted to Duke Hospital at the same time as the first patient. He also had been observed playing wih jimson-weed 8 hours previously, and the parents had noted flushing of the face and dilatation of the pupils 3 hours prior to admission. There had been no confusion, visual disturbance or ataxia. The physical examination revealed only a pulse of 150, a flushed face and dilated pupils. He was admitted overnight for observation, and received no specific treatment other than a tap water enema on admission. No signs of hyperactivity or depression were present during his 18 hour hospital stay. At the time of discharge the pupils were still dilated, but not as much as upon admission. Re-examination in 10 days revealed no abnormality.

CAMPHOR AND CAMPHORATED OIL

Camphor is present in some moth repellent cakes and balls as well as in camphorated oil. Camphorated oil is a 20 per cent solution of camphor in oil.

Early *symptoms* are headache, a sensation of warmth, excitement, nausea, vomiting and delirium. Camphor odor of the breath and urine is characteristic. The skin becomes clammy, and the face is alternately flushed and pale. The pulse is weak and rapid. Epileptiform convulsions may be followed by circulatory collapse.

Treatment is largely symptomatic, as with other central stimulants.

Gastric lavage and emetics are indicated if the patient is seen before the onset of severe symptoms. A short-acting barbiturate (e.g., sodium pentobarbital, 0.3 gm. intravenously), ether inhalations or chloral hydrate should be used to control convulsions. Opiates must be avoided. Artificial respiration may be necessary in case of respiratory failure.

CASE REPORT. An 18 month old boy was found with a bottle of camphorated oil at 8 A.M. Apparently there was very little missing from the bottle, but there was an odor of camphor on the child's breath, and he spat up some. Then he played normally all morning, and at 12:15 P.M. he was seized with convulsions which persisted. He was given 25 mg. of Demerol and fluids parenterally, and nasal oxygen was given en route to Duke Hospital The physical examination showed a temperature of 41.5° C.; pulse, 150; respirations, 28. The child was convulsing and slightly cyanotic. The head showed no lesions. The neck was supple. The ears, nose and throat showed no acute inflammation. There was conjugate deviation of the eyes to the right. The heart rate was rapid, the pulse 150 and forceful; there was a murmur. Loud tracheal rhonchi were heard in the chest. Abdominal examination was negative except for distention from swallowed air. Neurologically, the child was suffering generalized convulsions, but there was more clonus on the left side, with an increase in rigidity.

Accessory clinical findings were as follows: red blood cell count, 5,650,000; hemoglobin, 14.2 gm.; white blood cell count, 40,000, with a differential count of 93 segmenters and 7 lymphocytes. On the following day the white blood cell count was 21,600, with 75 segmenters, 1 stab form, 7 monocytes and 17 lymphocytes. Urinalysis showed 1 plus protein, 0 to 3 white blood cells per high power field, and many granular casts. The sedimentation rate was 24 mm. per hour, corrected. The cerebrospinal fluid on admission was clear, the pressure was normal, there were no cells, and the culture was sterile. A chest roentgenogram and fluoroscopy done on the fourth day revealed a cloudy density obscuring the right upper lung field, interpreted as representing a collapse of the right upper lobe.

On admission the child was immediately given a dose of Phenobarbital, and sponging was started to reduce fever. Open drop ether was necessary to stop the convulsions; with this treatment the child vomited a large amount of coffee ground material smelling of camphor; whereupon the stomach was lavaged with potassium permanganate and magnesium sulfate was instilled. During the first 40 hours the patient was on heavy Phenobarbital sedation and still having occasional short-lived tonic seizures of both sides. The right pupil remained dilated, while the left reacted to light. There was no evidence of consciousness at any time.

On the fourth day the child suddenly stopped breathing at noon, but respiration became regular again in one minute, but the left side of the chest did not move, and breath sounds came through poorly on that side. Tracheal intubation was done and suction performed; artificial respirations were kept up during this period. There was another episode of respiratory arrest that night, requiring the use of a respirator. No sedation was given during all this period. Respiratory distress continued to be the primary difficulty on the following day; a tracheotomy was performed at this time to deal with mucus adequately. During the last 6 to 8 hours of life constant artificial respiration with oxygen pressure bag via tracheotomy was necessary. Death occurred on the sixth day as a result of cardiac cessation, nonresponsive to stimulants.

MOTH REPELLENTS

Mothballs, repellent flakes and cakes most frequently contain paradichlorobenzene. Since halogenation of aromatic compounds decreases toxicity, ingestion of paradichlorobenzene rarely causes poisoning. However, prolonged exposure to paradichlorobenzene fumes will cause

liver damage and cataracts. Some repellents contain naphthalene alone or with paradichlorobenzene. A few contain camphor. As little as 2 gm. of naphthalene have caused fatal poisoning in a child, but the fatal dose in most cases is considerably larger.

Naphthalene poisoning should be treated with gastric lavage or emetics followed by the use of demulcents. Fluids should be given in large amounts orally and parenterally to decrease the concentration of the poison in the urine. During convalescence from severe intoxication the diet should be high in carbohydrate and vitamins, moderately high in protein, but low in fats to promote regeneration of liver tissue. Several cases of hemolytic anemia have been reported following the ingestion of and exposure to this agent.

ANILINE DYES

Reports of aniline dye poisoning among infants are fairly numerous. All the patients except one have been newborn infants poisoned by contact with diapers freshly stamped with material containing the dye. Several instances of paranitraniline poisoning from the ingestion of waxed crayons (red and orange) have been reported. Aniline dye poisoning may cause severe degrees of cyanosis due to methemoglobinemia. The infants are apathetic, gasp for air, and may have convulsions. Treatment consists in removing the source of the dye immediately and placing the infant in an oxygen box. If the cyanosis is alarming, methylene blue should be given.

DDT

Dichloro-diphenyl-trichloro-ethane (DDT) is used in spray guns and insecticide "bombs." An adult ordinarily sprays well below his own nose, and the mist may float at just the right plane for inhalation by a child. The vehicle is often kerosene, which may act synergistically in causing symptoms. In mild cases only symptomatic treatment is required. In acute intoxication control of convulsions is the first consideration. Barbiturates have been used for this purpose. Calcium gluconate has been recommended for control of hypocalcemia. Administration of oil is contraindicated because it increases absorption.

FERROUS SULFATE

The effects of large amounts of ferrous sulfate on small children are pallor, vomiting (hematemesis in some instances), tachycardia, drowsiness and restlessness. The stomach should be lavaged with sodium bicarbonate, leaving 5 to 10 ounces in the stomach. Bismuth

carbonate, 0.2 gm. (3 grains), is given every four hours. Fluids and transfusions are indicated for shock.

MUSHROOM (INEDIBLE), TOADSTOOL

In this country almost all cases of mushroom poisoning are caused by fungi of the Amanita genus, particularly *Amanita muscaria* and *Amanita phalloides*—commonly referred to as toadstools. Treatment consists in gastric lavage with tannic acid 1:200 or potassium permanganate 1:1200 followed by a saline purgative. Atropine sulfate given subcutaneously in a dose of 0.1 to 0.5 mg. (1/640 to 1/120 grain) specifically antagonizes the overstimulation of the parasympathetic nervous system caused by muscarine. A high protein diet and protein hydrolysate administered intravenously help prevent the severe liver damage caused by phalloidin. Supportive therapy should be given as required.

NICOTINE

Severe poisoning from eating tobacco in the form of cigarettes, cigars, snuff, and the like, is believed to be rare because the child soon vomits. However, certain insecticides contain nicotine and may be ingested, causing severe intoxication. Gastric lavage should be administered immediately, using solutions of gallic acid, tannic acid or potassium permanganate. Emetics, a magnesium sulfate purge and activated charcoal are recommended. Use the necessary supportive measures: oxygen, artificial respiration, stimulants and shock preventives. Do *not* administer strychnine.

ORGANIC PHOSPHATE (INSECTICIDES)

Parathion, TEPP, HETP and E-838 are recently introduced insecticides that were developed by the Germans during World War II while they sought highly lethal "nerve gases" for use in chemical warfare. It is highly important that the medical profession realize the widespread use by farmers, florists and commercial sprayers of these phosphate insecticides and be informed of the toxic symptoms they cause in man.

The *symptoms* are due to muscarine-like, nicotine-like and central nervous system effects like those of physostigmine which are attributable to the accumulation of acetylcholine. Gastrointestinal disturbances, sweating, salivation, miosis, involuntary defecation and urination, confusion, muscle weakness and generalized convulsions comprise the list.

Atropine, although specific against the parasympathetic effects of the poison, does not help the muscular weakness. Therefore artificial respiration may be required for many hours. Suction to clear the airways and positive pressure oxygen should be given if pulmonary edema occurs. Respiratory depression contraindicates the use of morphine.

DEODORANTS

Deodorants are usually a solution of an aluminum salt and are practically harmless. Depilatories contain barium or sodium sulfide, which is fairly innocuous. However, thallium acetate, which has been used in depilatories, is very toxic, causing severe gastrointestinal and cerebral symptoms. *Treatment* should consist in lavage with sodium thiosulfate, calcium by mouth, and sodium thiosulfate by vein.

PHOSPHORUS POISONING

Phosphorus poisoning may occur from eating rat poison or from certain fireworks such as the giant torpedoes. Matches do not contain the dangerous form of phosphorus at the present time. The gastrointestinal *symptoms* are similar to those reported with sodium fluoride poisoning. Hematemesis may be severe. In the later stages cardiac and respiratory failure develops, sometimes accompanied by delirium, coma and death.

Oily or fatty materials such as milk should never be given these patients, since they aid the absorption of phosphorus. Prompt lavage with a 1:5000 solution of potassium permanganate will change the poison to innocuous phosphoric acid; irrigation should be continued until the returning fluid is clear. Some magnesium sulfate should be left in the stomach. Intravenous glucose and molar lactate solutions should be given as necessary for acidosis.

STRYCHNINE POISONING

Strychnine poisoning, although not as common now as in the past, is still responsible for many deaths in children. Bright-colored, sugar-coated cathartics and tonic tablets are responsible. Hinkle's Cascara tablets with strychnine sulfate (1/60 grain, or 0.001 gm.), A.B.S. tablets (aloes, belladonna and strychnine), Alophen pills and many others are left carelessly about where children can get hold of them. The symptoms develop in one to three hours, depending on the solubility of the tablets. The convulsions resemble the convulsions associated with tetanus.

Treatment. Control the convulsions with intravenous sodium pentobarbital or Avertin by rectum. Avoid lavage until the convulsions are controlled; then lavage the stomach with a 1:5000 solution of potassium permanganate or a tannic acid solution. Give activated charcoal in water by mouth or stomach tube. Start supportive therapy where necessary, such as artificial respiration and oxygen.

BORIC ACID POISONING

Boric acid poisoning has received considerable publicity of late, and there is no question that its indiscriminate use over large areas of broken skin or mucous membranes is dangerous. However, the small amount present in baby powders, used mainly as a buffering and fungistatic agent, is safe for normal use. The *symptoms* of boric acid poisoning are erythema and exfoliation of the skin, vomiting, inanition, dehydration and convulsions. *Treatment* consists in removal of the source of boric acid, parenteral fluids and barbiturates to control the convulsions.

GENERAL PRINCIPLES OF TREATMENT

In handling cases of acute poisoning the following principles should be kept in mind:

1. Identify the poison as soon as possible, so that specific measures may be promptly instituted. The label on the container, if still present and legible, will give the ingredients and may also list specific antidotes. A telegram or telephone call to the manufacturer for identification may be necessary.
2. Remove the bulk of the poison from the stomach by gastric lavage or an emetic.
3. Administer an antidote for the residual poison not removed by gastric lavage. When a stomach tube is used, leave the antidote and other remedies in the stomach before removing the tube.
4. Give an antagonist when available.
5. Administer symptomatic treatment as indicated.
6. When the nature of the poison is unknown, one may safely give the "universal antidote":

UNIVERSAL ANTIDOTE

Pulverized charcoal (burnt toast)	2 parts
Magnesium oxide (milk of magnesia)	1 part
Tannic acid (strong tea)	1 part

One gram of charcoal will absorb 40 mg. of phenol and more than 500 mg. of strychnine. The tannic acid precipitates alkaloids, certain glucosides and many metals. The magnesium oxide neutralizes acids.

Antidotes are given after ingestion of poison only to render it inert or prevent its absorption by changing its physical nature. In general, soap or milk of magnesia may be used in poisoning due to acids; vinegar, orange or lemon juice after ingestion of alkalies. Sodium thiosulfate, 15 gm. in 2 liters, is recommended for heavy metals. Intoxication due to alkaloids such as atropine or morphine is combated with solutions of potassium permanganate 1:5000 or tannic acid 0.5 per cent.

BAL

BAL (2,3-dimercaptopropanol, British anti-lewisite) is a good antidote for mercury, arsenic, gold and cadmium poisoning. It is less effective for lead and silver, and practically ineffective if tissue damage is extensive. It should, therefore, be given as soon as possible, and its administration should be continued until the urinary excretion of the metals is at a minimum. The dosage recommended is 3 to 4 mg. per kilogram intramuscularly every three to four hours. Since this amount is about half the toxic dose, undesirable side effects are encountered. These include lacrimation, salivation, nausea, vomiting, fall in blood pressure, and pulmonary edema. The previous administration of ephedrine may alleviate many of these symptoms.

PREVENTION

The prevention of poisoning requires protection and education. Although protection is paramount in the age group most frequently involved, effective educational experiences adapted to the child's level of development may further decrease the risk. Parents can profit even more from education. The physician's educational use of a home check list of poison hazards may succeed with those deaf to all medicines in a locked closet, no inflammable liquids and no cleaning or polishing materials on lower shelves or floor and no penny-pinching saving of solvents and insecticides in "pop" bottles. Unfortunately, physicians are often culpable of their tacit approval of many home remedies of dubious worth. Moreover, we do not familiarize ourselves with the contents of our own various household agents. An even more glaring fault is bringing home samples, many of them containing new toxic drugs, of which we are totally ignorant. All these precautions require eternal vigilance, but it is worth the price. Collectively, as a group, we physicians can work for more stringent State and Federal laws to prevent these tragic accidental poisonings.

REFERENCES

1. Aikman, J.: Pediatric Emergencies. Pediatrics, 2:209, 1948.
2. Arena, J. M.: Accidental Poisoning in Children. N. C. Med. J., 9, December 1948. (Reprinted Mod. Medicine May 1, 1949.)
3. Arena, J. M.: Accidental Poisoning in Children. Ciba Clinical Symposia, 3, April-May 1951.
4. Arena, J. M.: Miscellaneous Poisons, Acute, in Conn, H. F., ed.: Current Therapy. Philadelphia, W. B. Saunders Company, 1954.
5. Binder, I.: Lead Encephalopathy: Treatment and Recovery. Report of Case. Arch. Pediat., 67:51, 1950.
6. Bodansky, O.: Mechanism of Action of Methylene Blue in Treatment of Methemoglobinemia. J.A.M.A., *142*:923, 1950.
7. Carver, G. M., Jr., Arena, J. M., and others: Clinic on Poisoning. J. Pediat., 32: 207, 1948.
8. Chittenden, R. F., and Mapes, R.: Poisoning in Childhood. California & West. Med., 56:137, 1942.
9. Clark, Esther B.: Poisoning Due to Ingestion of Wax Crayons. J.A.M.A., *135*: 917, 1947.
10. Comly, H. H.: Cyanosis in Infants Caused by Nitrates in Well Water. J.A.M.A., *129*:112, 1945.
11. Dubow, E., and Solomon, N. H.: Salicylate Tolerance and Toxicity in Children. Pediatrics, 1:495, 1948.
12. Fashena, G. J., and Walker, J. N.: Salicylate Intoxication. Am. J. Dis. Child., 68:369, 1944.
13. Gold, H.: Conference: Household Poisonings. Am. J. Med., 6:237, 1949.
14. Gold, H.: Conference: Household Poisonings. II. Am. J. Med., 8:372, 1950.
15. Graubarth, J., Bloom, C. J., Coleman, F. C., and Solomon, H. N.: Dye Poisoning in the Nursery. J.A.M.A., *128*:1155, 1945.
16. Johnson, G., Kurz, A., Cerny, J., Anderson, A., and Matlack, G.: Nitrate Levels in Water from Rural Iowa Wells: A Preliminary Report. J. Iowa M. Soc., 36:4, 1946.
17. Kernodle, G. W., Taylor, G., and Davison, W. C.: Lye Poisoning in Children. Am. J. Dis. Child., 75:135, 1948.
18. Lesser, L. I., Weens, H. S., and McKey, J. D.: Pulmonary Manifestations Following Ingestion of Kerosene. J. Pediat., 23:352, 1943.
19. Longscope, W. T., and Luetscher, J. A., Jr.: The Use of BAL (British Anti-Lewisite) in the Treatment of the Injurious Effects of Arsenic, Mercury and Other Metallic Poisons. Ann. Int. Med., 31:545, 1949.
20. Lueck, W. W.: Poisoning in Children: Newer Methods of Treatment. Journal-Lancet, 69:155, 1949.
21. Rohwer, S. A., and Haller, H. L.: Pharmacology and Toxicology of Certain Organic Phosphorus Insecticides; General Description of Their Activity and Usefulness. J.A.M.A., *144*:104, 1950.
22. Rosenfield, A. B., and Huston, R.: Infant Methemoglobinemia in Minnesota Due to Nitrates in Well Water. Minnesota Med., 33:787, 1950.
23. Smith, N. J.: Death Following Accidental Ingestion of DDT. J.A.M.A., *136*: 469, 1948.
24. Stocken, L. A., and Thompson, R. H. S.: Reaction of British Anti-Lewisite with Arsenic and Other Metals in Living Systems. Physiol. Rev., 29:168, 1949.

Duke University Hospital
Durham, N.C.

HEAD INJURIES IN CHILDREN

WILFRED PICKLES, M.D.

THOMAS C. MC OSKER, M.D.

Head injuries in children are of such common occurrence and the tragic results which may follow apparently minor damage are so well known that the proper handling of a patient who has sustained a blow on the head constitutes a real problem. In many instances, of course, the condition of the patient obviously demands hospital treatment, but in a great many more the indications are not clear. It is evidently impractical and unnecessary to send to a hospital every youngster who gets a bump on the head. What, then, should guide us in determining which patients have injuries with possible serious implications, and which may safely be treated at home?

OFFICE VERSUS HOSPITAL TREATMENT

The first consideration is an estimate of the condition of the patient as a whole. If he has a weak, thready pulse, a lowered blood pressure and cold, clammy skin, he is in a state of circulatory depression or traumatic shock; if he has a cool skin and lowered rectal temperature, he is in a state of incipient shock; in either case he should be kept warm and transported at once to a hospital with a minimum amount of handling. A careful neurologic examination should be done and any significant abnormalities noted. Any loss of consciousness, particularly one coming on some time after the accident, drowsiness, apathy, nausea, vomiting or persistent headache may indicate possible serious injury. Bleeding from the ears, nose or pharynx not explained by local injury, evidence of blood behind an intact ear drum or

From the Department of Neurosurgery, Rhode Island Hospital, Providence.

discharge of cerebrospinal fluid from any orifice suggests a compound basal skull fracture. If any of these conditions is present, hospitalization is advisable.

OFFICE TREATMENT

In the absence of such signs, treatment in the home or office can be carried out. *Laceration of the scalp* should be treated by shaving a wide area about it and infiltrating this area with procaine. A gloved finger should then be inserted in the wound to determine the presence or absence of underlying fracture or foreign body. If these are not found, the wound should be débrided and washed out thoroughly with saline solution and then, after all bleeding has been controlled, closed without drainage with interrupted silk stitches.

Lacerations of the face can be treated in a similar fashion; if they are at all extensive, however, a better cosmetic result can usually be obtained by doing the repair in a well equipped operating room. Either tetanus toxoid or antitoxin should, of course, be given after such injuries.

Abrasions of the scalp and face can be treated by the use of a bland ointment; if they contain ground-in dirt, however, they should be scrubbed well with a stiff brush and soap and water, with some form of anesthesia. It should not be forgotten that extensive, dirty abrasions carry as much risk of infection with tetanus as do lacerations.

Hematomas of the scalp may be alarming to the parents and confusing to the attendant, since they often develop a raised border under the skin which, on palpation, is often indistinguishable from a depressed skull fracture. A tangential film will rule out such a fracture, however, and the hematoma is then best treated by leaving it alone. It will usually persist, with some softening, but no particular change in size, for about two weeks, after which it is rapidly absorbed. The only indication for opening such a hematoma is the rare development of infection from an overlying abrasion or laceration.

The careful practitioner will often have x-ray examinations made on children who have suffered apparently minor head injuries. The discovery of a *linear fracture* under such circumstances is not, of itself, a reason for sending the child to the hospital; if none of the indications mentioned is present, a three week period of rest at home under careful observation is adequate and proper treatment. Failure to show a skull fracture by roentgenogram should never be used as a reason for refusing admission to a hospital of a child with a head injury. This is, unfortunately, still frequently done, whereas the decision should rest on the clinical findings.

HOSPITAL TREATMENT

Traumatic Shock

When the patient is admitted to the hospital, the first thing to be determined is the presence or absence of traumatic shock. It is our practice to record half-hourly observations of the temperature, pulse, respiration and blood pressure. We were formerly troubled by the development of delayed shock in many patients; the blood pressure would hold up well for a considerable period and then fall sharply between observations, with the immediate development of clinical shock. A study of the charts kept on these patients showed that they had one thing in common—a steadily falling rectal temperature. It is now our practice to start shock treatment when this falling temperature becomes apparent, and since we have followed this rule we have had no instance of delayed shock. The significance and seriousness of traumatic shock are not always appreciated, but further acquaintance with this state of circulatory depression will develop in one a profound respect for its dangers; delay in treatment may well render the changes irreversible, and the patient may then die of shock alone.

Shock is treated by the use of heaters and blankets to conserve body heat, the intravenous administration of fluids and blood and the avoidance of all unnecessary manipulations. If the patient enters in shock, he is put to bed at once without being undressed, and examination is limited so as to avoid exposure. Caffein sodium benzoate may be given in the muscles; if there is no abdominal injury, hot coffee given by rectum is of value. No roentgenograms are taken, no lumbar puncture is done, and, with rare exceptions, no operative procedure is undertaken until circulation is re-established. In very severe shock we have recently tried the use of Levofed, but in our hands it has proved of no value in changing the outcome.

When shock has been overcome, the patient is given a complete physical and neurologic examination. If, as often happens, injuries to other parts of the body are discovered, arrangements for their proper care are made. Our chief interest lies in the determination of the degree and severity of brain damage and the discovery of complications such as bleeding within the head and injuries of the skull. We follow, in the main, the classification devised by Munro,[1] dividing brain damage into three classes: concussion, congestion, and contusion. It must be recognized, of course, that degrees of injury merge imperceptibly from one to another and that any classification is arbitrary; but for purposes of description and study, it is useful to have some standards to follow.

Brain Concussion

The term "concussion of the brain," or "commotio cerebri," has been and still is used by many to indicate brain damage of any degree. In this classification its use is limited to those patients having immediate loss of consciousness of relatively short duration with complete recovery and no sequelae. This definition limits the diagnosis to a very small group, about 4 per cent of our series. No organic injury to the brain is demonstrable and, after the recovery of consciousness, there are no neurologic signs or symptoms. Lumbar puncture gives entirely negative findings: the initial pressure varies with the age of the patient from 100 to 150 mm., with normal fluctuations with pulse, respiration and straining; the cellular content is normal; and the protein content varies with age from 20 to 40 mg.

The *treatment* of this condition consists in bed rest, observation and proper nourishment. We were formerly insistent that such patients remain in the hospital for ten days; with increasing costs and the shortage of beds we have been compelled to modify this to a certain degree, but we still try to arrange for such a rest period at home after hospital observation has made it reasonably certain that complications will not develop. There are those who feel that prompt ambulation is better for the patient; observation of children treated in this manner leaves us strongly convinced that a fairly long initial period of complete physical rest does much to reduce annoying and sometimes disabling late sequelae.

Brain Congestion

In congestion of the brain we have an actual swelling within the tight confines of the dura, and this is shown clinically by headache, nausea and vomiting, drowsiness, apathy or irritability. Neurologic examination gives no abnormal findings. Examination of the fundi usually shows no evidence of papilledema, but with severe congestion there may be some venous engorgement. Choking of the disks develops slowly in increased intracranial pressure and lags six or seven days behind its onset; increase in the size of the blind spots is a much more prompt and sensitive index and may be of great value when the use of lumbar puncture is inadvisable, as in patients with suspected intracranial bleeding or compound basal skull fracture. Spinal tap gives normal findings except for increase in the initial pressure. If this increase is marked, it may be safely reduced by removing enough fluid to bring the pressure halfway to the normal.

There must be some marked difference in the conditions existing in chronic pressure increase, such as that met with in brain tumors, and the acute increase found with trauma; we should be unwilling to reduce pres-

sure in this way in the chronic state, but we have never seen the development of a medullary pressure cone following this procedure in an acute head injury. Repeated taps may be made if the pressure persists and the resulting symptoms make them necessary. We have tried other methods of reducing intracranial pressure, including mild to severe limitation of fluid intake, the intravenous use of sugar solutions and the intramuscular use of magnesium sulfate; none of these has proved to have lasting value, and we have given them up. In acute general edema of the brain, however, we have sometimes seen striking results with the use of intramuscular caffeine.

Brain Contusion

In contusion of the brain, under which term we include laceration, there is an actual bruising or tearing of the brain substance. Mild contusion may be indicated by lack of knowledge of the events concerned with the accident or of occurrences prior to the injury, a condition known as retrograde amnesia; and consciousness may or may not be lost. In the more severe states there may be prolonged unconsciousness extending to semicoma or complete coma, with no response to any stimuli. The patient may be very quiet, with no spontaneous movement, or he may be wildly excited and thrashing about. Convulsions are not common, but may occur, and they are usually general. Respiration may be quiet and easy, or it may be labored and stertorous or even become Cheyne-Stokes in character. Focal signs of irritation or depression are common, and the shifting nature of these signs is typical of brain contusion. Sphincter disturbances are not uncommon. Lumbar puncture usually shows some increase in initial pressure, but some patients with severe contusion may have a normal or even a lowered pressure. Red blood cells in the cerebrospinal fluid may vary from none to a large number. The protein content is elevated. The presence of a moderate number of red cells in the fluid does not explain a marked rise in the protein level; a convenient method of determining their effect is the realization that 750 red cells, with their surrounding plasma, will account for a protein rise of 1 mg.

Treatment. The treatment of contusion will, as can be readily appreciated, vary with the severity of the condition. Patients with mild contusion are treated in much the same way as those already considered; those with severe injury demand much more careful handling. Excitement or a tendency to convulsions is cared for by sedation, usually by sodium luminal intramuscularly, and occasionally with pentobarbital, chloral hydrate or paraldehyde by rectum. We avoid the use of morphine and its derivatives and substitutes, since they seem to depress respiration and to increase intracranial pressure; when the control of

pain is a problem, it can usually be obtained by a combination of barbiturates and acetylsalicylic acid compound. If respiration is embarrassed or the color is poor, oxygen is given by nasal catheter or with a Burgess box; in fact, the use of oxygen seems to be of considerable value even if there is no evident respiratory difficulty. The lungs, which are prone to get in trouble from inhalation and immobility, should be protected by frequent suctioning of the upper air passages and the prophylactic use of penicillin. But the chief effort must be directed to the maintainance of as nearly normal general physiology as possible, so that nature may be given an opportunity to heal the brain damage.

The normal daily fluid requirement, as indicated by the patient's age and weight, and with due allowance for unusual losses from overventilation or sweating, should be given by mouth or vein. If the patient is unable to swallow, he can be given fluids, salt, part of his caloric needs in the form of dextrose, and vitamins intravenously. After three or four days, however, replacement of protein must be undertaken. We have tried numerous intravenous protein preparations, but to date we have found none which will maintain protein balance. When the patient remains unable to swallow for this length of time, we accordingly undertake feeding by stomach tube. We have used indwelling tubes, including the newer, small plastic tubes, but we have found that some degree of tracheal irritation always results. Our present routine is to pass a rubber stomach tube about 10 A.M. and to insert through it half of the daily food requirement, including all needed elements. The tube is then clamped off, and about 3 P.M. the remainder of the mixture is given, and the tube is withdrawn. Care must be taken that none of the mixture enters the breathing passages, but this can be done without undue difficulty. One great advantage of this method is that the electrolyte balance is automatically maintained, and elaborate and sometimes confusing studies of this phase of the physiology are unnecessary. We have repeatedly carried patients along on this regimen for long periods; the longest time during which we have used it was for six weeks on a boy with severe brain contusion who eventually made a good recovery and is now back in school and is doing good work.

Proper bowel movements must be obtained, and this is usually accomplished by enemas or irrigation. If the patient is incontinent, an indwelling catheter is inserted and the bladder is emptied periodically; if the condition persists, some form of tidal drainage is set up. When an indwelling catheter is used, small doses of Gantrisin are given to control urinary infection.

Careful nursing care is essential, with meticulous attention to the dryness and cleanliness of the skin surfaces which have to sustain

pressure, and frequent changes of position; only in this way can the formation of bed sores be prevented. In considering the position of the patient it is well to remember that, though a flat, supine position is best for the patient in threatened or actual shock, later elevation of the head and chest is helpful in lessening pressure in the head and in protecting the lungs from congestion and infection.

Extradural Hemorrhage

Bleeding in the head is a serious complication of closed head injuries. The most serious and, fortunately, the least common is extradural hemorrhage. The classical description of this condition is well known. The patient is struck on the head and suffers an immediate loss of consciousness. In a short time he regains consciousness, only to lapse into unconsciousness again in a period varying from a few minutes to a few hours. He then has twitching movements, beginning in the face and extending to the arm and leg on the same side. These movements subside and are followed by weakness and eventual paralysis of the same areas. The child then sinks into coma and has a slow pulse and labored respirations. Later the pulse and temperature rise sharply and rapidly, and the patient dies.

This course of events is easily understood if the pathologic processes are appreciated. The initial loss of consciousness is due to concussion. The so-called lucid interval results from a recovery from the concussion. The secondary loss of consciousness results from bleeding from a torn middle meningeal artery with consequent increase of intracranial pressure. As the local pressure from the blood and clot increases, the cortex is at first irritated and then paralyzed, and these processes become evident as twitching and later loss of motor power on the opposite side of the body. As the general pressure continues to increase, the vital centers at the base of the skull become involved, and the patient dies from medullary failure.

Treatment. The onset of this condition constitutes a real surgical emergency, and immediate steps must be taken to correct it. This is one condition in which operation will not wait for the subsidence of traumatic shock. Immediate preparations for surgical exploration must be made. Blood must be ordered and shock treatment started, but the patient must be got to the operating room as quickly as possible. If the patient is unconscious, the operation can be performed under local anesthesia or with no anesthesia at all; if he is excited and active, intravenous barbiturates can be given, an endotracheal tube passed, and inhalation ether used if it is needed. If the clinical picture is as clear as that described above, the taking of roentgenograms to determine the presence of a linear fracture across the course of the artery

is unnecessary and a waste of valuable time. In any case such studies are not of too much value, for we have often seen such fractures without middle meningeal artery damage, and we have seen such damage without x-ray demonstration of a fracture; the decision as to the need for operation must be made on clinical grounds.

After the usual preparations a vertical transtemporal incision is made on the side opposite the clinical signs. The bone is entered with Hudson drills, and the opening is enlarged with rongeurs until it is about an inch in diameter. This results in the spontaneous extrusion of clot followed by brisk arterial bleeding. The temporary control of this bleeding may sometimes be difficult, but can usually be accomplished by pressure with cotton pledgets. The torn ends of the artery are then searched for, the opening in the skull being enlarged if more exposure is needed. When the ends are found, they are best and most securely closed by fine silk ties. If this is not possible, silver clips may be used or the vessel may be coagulated, but neither of these methods is as safe as the use of silk. If the vessel ends cannot be found, or if the proximal end is inaccessible, it may be necessary to raise the temporal lobe and pack the foramen spinosum with cotton and bone wax or with a sterile wooden plug. Blood, of course, must be replaced as the operation proceeds. When the bleeding has been controlled, the wound is closed with layers of interrupted silk stitches.

Occasional dramatic recoveries occur in patients operated upon without general anesthesia as soon as the pressure is released. The over-all mortality in this complication, however, is high and is largely due to concurrent brain damage, associated traumatic shock and delay in undertaking operation; it is usually considered to be about 50 per cent. The classical progression of symptoms is not infrequently incomplete; the lucid interval may not be noted or may be nonexistent, owing to overlapping of the processes involved or to the rapidity of the bleeding, and the signs of cortical irritation may be missed for similar reasons. Occasionally, extradural hemorrhage may result from stripping of the dura from the skull, with consequent venous bleeding; in this case the onset of symptoms is much slower and may take several days.

Acute Edema of the Brain

Extradural hemorrhage may be almost exactly simulated by an acute focal edema[2] of the cortex as a result of injury, and this focal process may be followed by acute general edema[3] simulating medullary compression from intracranial bleeding. A knowledge of this possibility is of considerable value, but it must not be used as an excuse for delay in preparing to operate. If, however, the patient improves markedly

while such preparations are being made, it is safe to wait with the expectation that spontaneous recovery may occur.

Subdural Hemorrhage

Subdural bleeding is not uncommon and comes from a tearing of the bridging veins extending from the pia to the large venous sinuses. If this bleeding is rapid, the condition may be indistinguishable from extradural hemorrhage, since it makes little difference physiologically whether the pressure is exerted from without or within the dura. This confusion in diagnosis does no harm to the patient, however, since exploration is indicated and the operation will reveal the true state of affairs.

If no extradural clot is found, the dura is opened and the underlying clot removed. It is usually unnecessary to control the bleeding, for it has commonly stopped by the time of operation. If it is persistent, however, it can be controlled by the use of Gelfoam strips.

Subdural Hematoma

The usual subdural hematoma develops more slowly and may or may not have localizing signs. If such signs develop slowly and are persistent, exploration is indicated. When, in a patient with recent head injury, the state of consciousness slowly worsens without focal signs, the development of a subdural clot must be suspected, and exploration should be carried out on both sides. In such cases the clot may be thick and the brain may not promptly resume its normal form to fill the space formerly occupied by the hematoma; in this event a rubber tissue drain may be inserted and left in place for thirty-six hours. If the brain fills the space promptly, no drainage is needed, but the dura is usually left open, and the remainder of the wound is closed with layers of interrupted silk stitches.

The slow development of signs in the average subdural hematoma is due to the fact that the brain is able to compensate for the pressure brought about by the original bleeding, but becomes embarrassed by further increase in the size of the mass by osmosis. This osmosis takes place through a membrane which gradually forms on the surface of the clot away from the dura, and much has been made of the necessity for the complete removal of this membrane at operation. It is our feeling that the only danger from the membrane comes from its ability to pass fluid into the highly concentrated substance of the clot; with the thorough removal of the clot the membrane becomes harmless. Its complete removal may involve the turning down of a large bone flap, considerable blood loss and traumatizing of the under-

lying brain, all without any compensating advantage. We have seen no harm result from leaving the membrane in place.

Subdural Hygroma

Symptoms similar to those resulting from a subdural hematoma may be brought about by a subdural hygroma, which is a collection of fluid in the same area, apparently due to a tear in the arachnoid; treatment consists in the evacuation of its fluid content.

Subarachnoid Hemorrhage

Subarachnoid bleeding is usually part of a generalized head injury with brain contusion, and has no characteristic signs other than the neck stiffness which accompanies any spillage of blood on the meninges. Subpial hemorrhage is rare, but can occur. It is usually mistaken for subdural bleeding and can be relieved by careful incision of the pia when it is found at operation. A subcortical hematoma occurs infrequently and gives signs and symptoms similar to those caused by subdural bleeding. It is practically never diagnosed prior to operation and is usually found with a ventricle puncture needle when an extradural or subdural hematoma is not found in the presence of strongly suggestive clinical indications. It is treated by incising the cortex with the electrocautery and allowing the clot to be extruded spontaneously.

Skull Fractures

Fractures of the skull constitute another complication which may or may not be serious. *Simple linear fractures of the vault* need give us little concern, for they heal by themselves and call for no specific treatment. *Depressed fractures of the vault* are commonly comminuted, and may involve one or both tables of the skull; they may result in focal irritative or paralytic signs if they press on the motor cortex, or they may be symptomless. They rarely call for emergency treatment, but are usually best elevated after the child is in good circulatory balance, even though they are causing no apparent trouble, to eliminate a possible later irritative focus.

A curved incision is made just beyond one edge of the depression, a scalp flap is turned back, and the depressed area is exposed; the bone involvement is usually considerably greater than the roentgenograms would lead one to believe. A bur hole is then made on the edge of the area, and an elevator is carefully introduced between the skull and dura. In infants and young children the skull is elastic and the depression can usually be snapped back into the normal position, where

it will remain. As the child grows older, the skull takes on the character of adult bone, and the fragments may be locked in the depressed position. In this event they may be freed by removing the impacted edges with fine rongeurs or DeVilbiss forceps, and they can then be replaced.

Compound fractures of the vault should be operated upon as soon as the child's general condition will tolerate surgery, and usually within six hours of the injury. The wound edges should be removed by sharp dissection, and all crushed and devitalized tissue should be removed. All bleeding should be controlled and the wound washed out well with saline solution. Not infrequently hair, particles of clothing or other foreign bodies have been driven into the wound. These should be searched for and removed. Bone fragments which are well attached and have good blood supply may be left in place; if they are completely detached or have lost their blood supply, they should be removed. The resulting bone defect usually becomes well covered with a dense connective tissue repair; if it is larger, and does not develop such protection, it can be covered later with a metal plate. If the dura has been torn and the brain exposed and torn, careful débridement and cleansing should be extended to these areas.

In depressed fractures in older children it is not uncommon for a vessel to have been torn and tamponaded by the bone fragments, and elevation of the bone results in brisk bleeding. This should be anticipated, and the vessel should be handled as in the case of the injured middle meningeal artery. When these procedures have been carried out, the dura should be closed if this is possible. If this cannot be done, owing to loss of tissue, the brain should be covered with Gelfilm and the wound closed over it, without drainage, with the usual layers of interrupted silk stitches.

The frontal sinus is often involved in these fractures. If the anterior wall alone is damaged, the wound should be débrided as described above, and this débridement should include the removal of the mucous membrane lining if it has been stripped from the bone or its viability is in question. The patency of the nasofrontal duct should be established by the passage of a probe, and the wound should then be closed without external drainage. If the injury involves the posterior wall as well, and there is a communication with the cranial cavity, this should be blocked by a water-tight closure accomplished by bringing together any available tissue with closely placed silk stitches, and the rest of the repair should be carried out as described before.

The control of infections in injuries of this sort has been given tremendous help by the use of sulfonamide drugs and antibiotics, but it must be remembered that the most important single factor in avoiding infection is still thorough débridement and careful mechanical cleansing

of the wound; without this essential preliminary the use of the newer agents will prove disappointing.

When there is bleeding from the ears, nose or pharynx not explained by local injury, or evidence of blood behind an intact ear drum, or drainage of cerebrospinal fluid from these areas, we must assume that the child has sustained a *compound basal skull fracture*. This diagnosis must be made on clinical evidence, in the main, since not over 10 per cent of such fractures are shown by roentgenogram. In general, no attempt should be made to block such bleeding or drainage, and the use of packing in the ears or nose should not be permitted, since it markedly increases the possibility of infection. If nasal bleeding constitutes a threat to life, packing may be used, but for as short a time as possible. Lumbar puncture is not done on these patients until ten days after the drainage has stopped; this precaution is taken to avoid possible reversal of flow and a consequent increased hazard of infection.

In our experience, compounding through the ear, unless there has been previous infection there, rarely results in central nervous system infection. Compounding through the nose, however, was formerly one of the most serious complications of head injuries, and all too often resulted in a fulminating meningitis for which we had no adequate treatment and which frequently had a fatal outcome in twenty-four to forty-eight hours. The introduction of the sulfonamide drugs changed all this, and they are still the best agents for the prevention and treatment of meningitis complicating this condition. It is now our practice to use penicillin intramuscularly for the avoidance of local infections, and appropriate doses of Gantrisin, by mouth or intravenously, to prevent meningitis. Since we have followed this regimen we have had no meningeal infection in compound basal skull fractures which we have cared for from their onset.

SUMMARY

Head injuries in children are common, and the problem of hospitalization is sometimes difficult of solution. In the main the decision should be made on clinical evidence rather than on x-ray demonstration of skull fracture. Traumatic shock or impending shock, indications of significant brain damage, signs and symptoms suggesting bleeding in the head, and clinical indications of depressed or compound skull fracture necessitate transfer to a hospital. After admission, treatment of shock takes precedence over almost all other considerations. When shock has been overcome, determination of the degree of brain damage and its treatment are undertaken. Concussion of the brain is treated by rest and observation for possible complications. Brain congestion is treated in much the same way, with lowering of intracranial pressure if

this is indicated. Contusion of the brain, if severe, demands painstaking attention to many details, the chief aim being the maintainance of as nearly a normal general physiologic state as possible, so that healing of the brain damage may take place. Bleeding in the head may be a serious complication in closed head injuries. Extradural hemorrhage is not common; when it does occur, it is a real surgical emergency and must have immediate treatment. Subdural hematomas are encountered fairly frequently and may be difficult of diagnosis; when discovered, they should be handled by removal of the clot. Subpial and subcortical hematomas are found rarely. Fractures of the skull present another major complication. Linear fractures of the vault, as such, need no treatment; depressed fractures in this area should be elevated. Compound fractures of the vault should have thorough débridement, careful cleansing, and elevation or removal of depressed fragments, while those at the base should be treated by measures aimed at the prevention of meningeal infection.

REFERENCES

1. Munro, D.: Cranio-cerebral Injuries: Their Diagnosis and Treatment. London, Oxford University Press, 1938, pp. 114–125.
2. Pickles, W.: Acute Focal Edema of the Brain in Children with Head Injuries. New England J. Med., 240:92, 1949.
3. Pickles, W.: Acute General Edema of the Brain in Children with Head Injuries. New England J. Med., 242:607, 1950.

184 Waterman Street
Providence, R.I. (Dr. Pickles)

MANAGEMENT OF THE ISOLATED CONVULSION

SAMUEL LIVINGSTON, M.D.

Clinical disturbances, including epilepsy, which are associated with convulsions constitute a group of the most frequent and challenging disorders encountered in the practice of medicine. Although such disorders are problems of all physicians, they are of prime importance to the general practitioner and the pediatrician, since over 90 per cent of convulsive disorders have their onset during the early years of life.

Many physicians in the past considered, and some even today still consider, a convulsion during early childhood an innocuous incident. This definitely is not always true. *A convulsion should be regarded as a serious sign until thorough examination of the affected child and the passage of time have proved it to be a symptom of some transient disease or a manifestation of some chronic illness such as epilepsy.* It is important, when considering the diagnosis of convulsions, to keep in mind that seizures are no more than manifestations of underlying disturbances which may be many and varied, as shown in Table 2. The arrival at an accurate diagnosis depends upon the correct interpretation of many factors gathered from the child's history, his examination and various laboratory procedures.

DISORDERS ASSOCIATED WITH CONVULSIVE SEIZURES

1. *A simple febrile convulsion* is a generalized seizure of short duration (averaging one to five minutes) which occurs soon after an elevation of temperature of variable degree. The fever is most frequently associated with an extracranial infection such as acute tonsillitis, otitis media, pharyngitis, and so forth. We do not regard convulsions occurring in association with infections (such as encephalitis, meningitis and

septicemia) which are known to invade the central nervous system as simple febrile convulsions.

2. *Congenital developmental diseases of the brain* such as cerebral aplasia, tuberous sclerosis, hydrocephalus and vascular anomalies, i.e., the Sturge-Weber syndrome.

3. *Intracranial infections* such as acute meningitis, encephalitis, cerebral abscess.

4. *Epilepsy* may be classified into two types: (1) cryptogenic (or idiopathic, or essential, or primary, or genuine, or true) and (2) sec-

TABLE 2. *Disorders Frequently Associated with Convulsive Seizures*

DURING THE NEONATAL PERIOD	AFTER THE NEONATAL PERIOD	
Cerebral birth injury	Epilepsy	Brain tumor
Extracranial infections (simple febrile convulsions)	Extracranial infections (simple febrile convulsions)	Acute head injuries
Intracranial infections	Intracranial infections	Breath-holding spells
Subdural hematoma	Subdural hematoma	Intracranial vascular disorders
Hypocalcemia (neonatal tetany)	Congenital developmental diseases of the brain	Congenital cerebral degenerative diseases
Kernicterus	Hypoglycemia	Lead poisoning
Congenital developmental diseases of the brain	Hypocalcemia	Hysteria
Hypoglycemia	(rickets—hypothyroidism)	Parasitic infestations
Epilepsy	Renal disorders	Drug intoxication

ondary (or organic, or symptomatic). The former type includes those convulsive disorders in which a specific cause cannot be determined; the latter type refers to those convulsive disorders which occur in association with or subsequent to known cerebral damage (toxic, traumatic or infectious).

A question we have been asked frequently by general practitioners is: Does the occurrence of a single seizure of undetermined etiology mean that such a patient has epilepsy, and, if so, should he be given daily anticonvulsant medication? Our answer to this question is as follows: A patient who suffers with a seizure and in whom a specific cause cannot be determined is regarded as having cryptogenic (or idiopathic) epilepsy until repeated examinations and passage of time have proved it to be a manifestation of some other disorder. If the electroencephalogram of such a patient presents specific abnormalities, we prescribe daily anticonvulsant medication. If, however, the electroencephalogram is normal, we do not administer daily anticonvulsant therapy unless the patient has a recurrence of a similar seizure. It must be noted that

the electroencephalogram is normal in many patients who suffer with definite clinical evidence of epilepsy, especially cryptogenic (idiopathic) epilepsy. Electroencephalograms were performed on 1803 of our 2224 patients with cryptogenic epilepsy. The brain wave pattern was normal in 520 (30 per cent) of these patients.[9]

5. *Breath-holding spells* are easily recognized, since the following triad of symptoms is seen in no other condition: (1) a precipitating factor such as a slight injury or some other minor provocative incident which evokes an acute emotional response; (2) violent crying ending suddenly in respiratory apnea; and (3) the occurrence of cyanosis, unconsciousness or convulsions, depending on the individual child and the duration of the apnea.

6. *Intracranial vascular disorders* such as cerebral vascular thromboses.

7. *Congenital cerebral degenerative diseases* such as Schilder's disease.

8. *Parasitic infestations* such as toxoplasmosis, cysticercosis, malaria, hydatid cyst.

HISTORY

When the physician is confronted with a child in a severe or protracted convulsion, he should immediately institute therapeutic measures to terminate the seizure. The immediate treatment of the convulsion itself is discussed later in this paper. Since, however, most of the convulsive seizures encountered in children are of short duration and terminated before medical treatment becomes available, the main problem in the management of the isolated convulsion, in most instances, is to discover and treat the cause.

The case history frequently gives important information. The physician should inquire whether the seizure was the first one the patient has had. If so, it is important to know whether there was an associated elevation of temperature, whether the child recently sustained an injury to the head, and so forth. The possibility of drug intoxication should be investigated. A history of similar convulsions in the past should always suggest the possibility of disturbances such as epilepsy, breath-holding spells, hypoglycemia, hypocalcemia, and the like. The age of the child should direct attention to certain disorders such as are listed in Table 2. In infants of less than one month of age cerebral birth injuries and neonatal tetany are relatively common causes for convulsions. Acute infections and epilepsy are the most common causes for convulsions in older children. The character of the seizure sometimes gives a clue to the nature of the underlying disturbances; e.g., a focal seizure should always suggest the possibility of a local lesion in the brain. It must be noted, however, that focal convulsions are also sometimes

encountered in patients in whom no evidence of pathology can be demonstrated. One hundred and two (5 per cent) of our 2224 patients with cryptogenic (idiopathic) epilepsy suffered with focal seizures.[9]

An elevation of temperature at the time of a convulsive seizure is generally indicative of an acute infectious process (extracranial or intracranial). Since convulsions occur frequently in young children in association with extracranial infections such as otitis media, tonsillitis and pneumonia, a careful search for such foci of infection should be made. If no evidence of an extracranial infection can be discovered or if signs or symptoms suggestive of an intracranial infection are present (stiff neck, Kernig's sign, and so on), a spinal puncture should be performed.

PHYSICAL EXAMINATION

A complete neurologic examination is imperative. Focal neurologic findings necessitate a careful search for a local cerebral lesion. A thorough funduscopic examination should also be made. Choked disks and engorgement of the retinal vessels are suggestive of increased intracranial pressure; retinal hemorrhages and choreoretinitis are suggestive of subdural hematoma and toxoplasmosis, respectively. Positive Chvostek, Trousseau and peroneal signs, carpopedal spasm and laryngospasm are strongly indicative of tetany. The presence of adenoma sebaceum or facial nevus vasculosus is presumptive evidence of tuberous sclerosis and the Sturge-Weber syndrome, respectively.

LABORATORY PROCEDURES

When the history or physical examination does not produce conclusive evidence of a specific diagnosis, the following laboratory procedures should be performed unless one can adequately exclude the condition of which the procedure under question is diagnostic.

Blood Examinations

A routine test for syphilis should be made.

Serum calcium, serum inorganic phosphorus and serum alkaline phosphatase should be evaluated. The normal total serum calcium is 10 to 12 mg. per 100 ml.; the normal serum inorganic phosphorus is 4.5 to 5.5 mg. per 100 ml.; and the normal serum inorganic phosphatase is 5 to 13 Bodansky units.

Studies of carbohydrate metabolism, such as fasting blood sugar determinations, glucose tolerance tests, insulin sensitivity and epinephrine

tolerance tests, should be made. The normal fasting blood sugar value is 60 to 120 mg. per 100 ml.

Blood lead level determinations are useful. Blood lead levels exceeding 0.06 mg. per 100 ml. are generally indicative of excessive lead ingestion.

The normal nonprotein nitrogen value of whole blood is 25 to 35 mg. per 100 ml.

Parasites should be searched for.

The blood should be cultured for organisms.

Urine Examinations

The urine should routinely be examined for protein and cellular elements.

Cerebrospinal Fluid Examinations

The cerebrospinal fluid should be examined in all patients who present the following findings: (*a*) those in whom the convulsive seizure is associated with clinical evidence of an intracranial infection such as meningitis or encephalitis; (*b*) those in whom the convulsive seizure is associated with an elevation of temperature and in whom the physical examination fails to reveal evidence of an extracranial infection (otitis media, tonsillitis or the like), even when there is no clinical evidence of meningeal or cortical irritation; (*c*) those who present signs or symptoms suggestive of a cerebral hemorrhage.

Normal cerebrospinal fluid values are as follows: cell count, 0 to 10 per cubic millimeter (predominantly lymphocytes); chlorides, 120 to 130 milliequivalents per liter; glucose, 50 to 80 mg. per 100 cc.; protein, 15 to 45 mg. per 100 cc. (lumbar); the Pandy test is negative.

Subdural Puncture

A subdural puncture should be performed when a diagnosis of subdural hematoma is considered. The signs and symptoms of a subdural hematoma are variable. It should always be suspected in a child in whom a week or more after a cranial injury there are complaints such as vomiting, headache of increasing severity, lethargy or symptoms suggestive of compression of the brain.

Electroencephalography

An electroencephalogram should be performed when a diagnosis cannot be established by the usual clinical and laboratory procedures.

Cranial Roentgenography

In the majority of instances roentgenograms of the head do not reveal any abnormality. However, as it is impossible to predict when such examinations will be of value, anteroposterior, occipital and stereoscopic lateral views of the skull should be taken routinely, if possible. Right and left lateral projections should be taken when it is impossible to obtain stereoscopic films. Direct roentgenographic examinations of the head will show the bony structures of the skull, any abnormal calcifications within it and significant asymmetries of the cranial bones.

Pneumoencephalography and/or cerebral arteriography should be performed on those patients in whom an intracranial neoplasm is suspected.

TREATMENT OF THE ISOLATED CONVULSION

The present discussion is devoted to the immediate treatment of the isolated convulsion. The reader may refer to the standard textbooks of pediatrics[1, 2, 4-7, 10] for the specific treatment of the various diseases such as meningitis, encephalitis, renal disorders, tetany, and others, which are known to be the cause of or associated with convulsions. He may also refer to books by Bridge,[3] Lennox,[8] Livingston,[9] Penfield and Erickson[11] and Putnam[13] for the treatment of epilepsy.

Prevention of Fatalities and Injuries

The convulsing child should be placed on a soft place and tight clothing loosened. Care should be taken to protect him from injuring himself during the violent movements of the attack. One of our patients broke his arm by striking it against a metal bedpost during a severe convulsion. Guards should be placed on the sides of the bed to prevent him from falling to the floor. It is usually advisable to place a padded tongue depressor or similar blunt object between the jaws to prevent biting of the tongue or cheek. Care should be taken that the patient does not aspirate food, vomitus or broken teeth. If possible, the patient should be kept on his side so that mucus and saliva will flow more freely from the mouth. *He should not be placed or be permitted to lie on his abdomen or back.* There should be no pillows in the bed. There are reports of patients who presumably died of suffocation caused by the head being buried in a soft pillow. We had one child who seemed to have suffered a considerable degree of anoxia from such a cause. Occasionally food or vomitus may so choke the air passages that suction becomes necessary. When anoxia becomes apparent, as often happens in greatly prolonged or frequently repeated convulsions, oxygen should be administered by inhalation to prevent cerebral damage.

Fortunately, most convulsions are of short duration and rarely endan-

ger the life of the patient directly. In the event of prolonged convulsions or status epilepticus, however, the condition must be considered a serious one. Status epilepticus refers to a state of recurring major motor seizures between which the patient does not completely regain consciousness. Under such circumstances the patient may sink deeper and deeper into a coma and become dehydrated and exhausted. Hyperthermia may also develop. Unless appropriate precautionary measures are carried out, death may follow. As in any other unconscious patient, it is necessary to maintain the fluid intake. This is usually best accomplished by clysis or intravenous administration of glucose and saline solutions. Catheterization may be necessary if the patient does not void spontaneously. Hyperthermia should be dealt with appropriately. Cool sponges, ice packs, ice bags and cool enemas are sometimes helpful. In status epilepticus or prolonged convulsions lasting over forty-eight hours, prophylactic antibiotics such as penicillin should be administered to prevent secondary infection.

Termination of the Attack

Caution must be exercised to avoid doing more harm than good. *Morphine or opium derivatives must never be used.* These drugs depress the respiratory center and cough reflex and also sometimes mask important diagnostic signs and symptoms. Counterirritation procedures, such as mustard baths or packs and hot baths, are to be discouraged because they are ineffectual. Cool sponges, ice packs, ice bags or cool enemas are sometimes helpful in those patients in whom there is an elevation of temperature associated with the convulsion. It is not safe, from the viewpoint of possible cerebral damage by the convulsion itself, to allow the seizure to continue too long. Anticonvulsant therapy should be administered as soon as feasible. Diagnostic procedures such as spinal or subdural punctures should not be performed until after the administration of anticonvulsant therapy. Therapeutic measures which may mask diagnostic findings should not be instituted until appropriate tests necessary for the correct diagnosis have been carried out. For example, calcium should not be administered to a child in whom a hypocalcemic convulsion is suspected or glucose to one in whom a hypoglycemic convulsion is suspected, until samples of blood have been obtained. Once the specimens of blood have been drawn, calcium or glucose, as indicated, may be administered before the results of the blood examinations are known.

In the event of a severe or protracted convulsion it is advisable to administer one large dose of phenobarbital, using the water-soluble form of the drug (sodium phenobarbital). Sodium phenobarbital is prepared in sterile powders and tablets. The sterile powder is available in ampules

containing 130 mg. (2 grains) and 320 mg. (5 grains). The sterile tablets are available in doses of 32 mg. (½ grain) and 65 mg. (1 grain). Either the powder or tablet can be quickly disolved in sterile warm water for injection. The doses of sodium phenobarbital to be administered subcutaneously to the average-sized child are given in Table 3.

TABLE 3. *Average Dose of Sodium Phenobarbital to Be Administered Subcutaneously for the Control of Severe and Protracted Convulsive Seizures*

AGE OF PATIENT	METRIC*	APOTHECARY*
Under 1 year	32–65 mg.	½–1 grain
1–2 years	65–130 mg.	1–2 grains
2–3 years	130–200 mg.	2–3 grains
3–4 years	200–230 mg.	3–3½ grains
4–5 years	230–260 mg.	3½–4 grains
Over 5 years	260 mg.	4 grains

* The conversion of the metric system of weights to the apothecary system is approximate.

We have also found Seconal, administered by the rectal route, to be helpful in some cases. Seconal is available in capsules of 50 mg. (¾ grain) and 100 mg. (1½ grains) and in suppositories of 130 mg. (2 grains). We prefer the capsule form. It is advisable to prick several pinpoint holes in the capsule and insert it high up into the rectum. It is important that the capsule not be inserted into a fecal mass, since absorption will be much delayed. After the capsule has been inserted into the rectum the buttocks should be taped with adhesive so that the capsule will not be easily expelled. The doses of Seconal to be admin-

TABLE 4. *Average Dose of Seconal to Be Administered Rectally for the Control of Severe and Protracted Convulsions*

AGE OF PATIENT	METRIC*	APOTHECARY*
Under 1 year	50–100 mg.	¾ grain–1½ grains
1–2 years	100–150 mg.	1½–2¼ grains
2–3 years	150–200 mg.	2¼–3 grains
3–4 years	200–250 mg.	3–3¾ grains
4–5 years	250–300 mg.	3¾–4½ grains
Over 5 years	300 mg.	4½ grains

* The conversion of the metric system of weights to the apothecary system is approximate.

istered rectally to the average-sized child are given in Table 4. *When large doses of sedatives are used, the patient should be observed carefully for marked depression of respiration.*

If the seizure does not stop within twenty to thirty minutes after the administration of the recommended doses (see Tables 3 and 4) of

phenobarbital or Seconal, vinyl ether or chloroform inhalations should be given. In the event of an acute disease of the respiratory tract, ether should not be used except in extreme emergencies.

We have found the foregoing therapeutic regimen to be satisfactory for the control of most convulsions. The following are some other procedures which may also be used: the intravenous administration of sodium phenobarbital, 65 to 130 mg. (1 to 2 grains), or sodium amytal, 65 to 320 mg. (1 to 5 grains), and paraldehyde by rectum in doses of 0.3 cc. (5 minims) per kilogram every four to six hours with cottonseed or olive oil. Intravenous and intramuscular paraldehyde has also been used.[14, 15] It has been our experience that the intravenous or intramuscular administration of paraldehyde is no more effective than rectal administration. Chloral hydrate (10 per cent) may also be given as follows: 50 mg. (0.5 cc.) per kilogram by rectum with cottonseed oil or by mouth with a sweet diluent such as orange juice or Coca-Cola. The total dose should not exceed 10 cc. (1 gm.). This dose may be repeated in an hour if the desired effect is not obtained. Peterman[12] recommends Avertin (tribromoethanol), 75 mg. per kilogram by rectal instillation. The intravenous use of Pentothal sodium is also advocated. This drug, however, should not be given except by an experienced anesthetist and preferably under hospital conditions, where oxygen therapy and other means of resuscitation are readily available.

The data presented in this paper are taken in part from the author's textbook: The Diagnosis and Treatment of Convulsive Disorders in Children.[9]

REFERENCES

1. Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923.
2. Brenneman, J.: Practice of Pediatrics, edited by I. McQuarrie. Hagerstown, Md., W. F. Prior Company, 1948.
3. Bridge, E. M.: Epilepsy and Convulsive Disorders in Children. New York, McGraw-Hill Book Company, Inc., 1949.
4. Davison, W. C.: The Compleat Pediatrician. 6th ed. Durham, Duke University Press, 1949.
5. Grulee, C. G., and Eley, R. C.: The Child in Health and Disease. 2d ed. Baltimore, Williams & Wilkins Company, 1952.
6. Holt, L. E., Jr., and McIntosh, R.: Holt's Diseases of Infancy and Childhood. 12th ed. New York, Appleton-Century-Crofts, Inc., 1953.
7. Hughes, J. G.: Pediatrics in General Practice. New York, McGraw-Hill Book Company, Inc., 1952.
8. Lennox, W. G.: Science and Seizures. 2d ed. New York, Harper & Brothers, 1946.
9. Livingston, S.: The Diagnosis and Treatment of Convulsive Disorders in Children. Springfield, Ill., Charles C Thomas, 1954.
10. Nelson, W. E., ed.: Textbook of Pediatrics. 6th ed. Philadelphia, W. B. Saunders Company, 1954.
11. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization. Springfield, Ill., Charles C Thomas, 1941.

12. Peterman, M. G.: Convulsions in Childhood. Am. J. Dis. Child., 72:399, 1946.
13. Putnam, T. J.: Convulsive Seizures. 2d ed. Philadelphia, J. B. Lippincott Company, 1945.
14. Wechsler, I. S.: Intravenous Injections of Paraldehyde for the Control of Convulsions. J.A.M.A., *114*:2198, 1950.
15. Whitty, C. W. M., and Taylor, M.: Treatment of Status Epilepticus. Lancet, 2:591, 1949.

601 North Broadway Avenue
Baltimore 5, Md.

EMERGENCIES OF THE RESPIRATORY TRACT IN INFANTS AND CHILDREN

GEORGE B. LOGAN, M.D.

Diseases of the respiratory tract in children which require urgent treatment usually are manifested by difficulty in breathing. The symptoms, so alarming to parent and patient, must be appraised quickly and accurately by the physician when he first sees the patient. Measures for their relief must be instituted promptly.

In children, especially infants, the air passages are small in caliber, so that small quantities of secretion or aspirated material and minimal edema may produce considerable difficulty in breathing.

This paper will deal chiefly with diseases which produce obstruction in the tubular air passages rather suddenly. Two important causes of obstruction, discussed in detail by others in this symposium, will be dealt with herein only by name: dyspnea of the newborn and aspiration of foreign bodies. Pneumonia will be dealt with briefly, as will sudden death, tracheo-esophageal fistula, respiratory problems associated with poliomyelitis, pneumothorax and asphyxial states induced by drowning, electric shock and inhalation of noxious gases.

OBSTRUCTIVE LESIONS

When the physician is confronted with a child who has an obstructive lesion of the respiratory tract, it is imperative that not only the cause of the obstruction be learned, but also its location. Obstruction at various levels produces symptoms that are both similar and dissimilar (Table 5).

From the Section of Pediatrics, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

TABLE 5. *Signs and Symptoms of Obstructive Diseases of the Respiratory Tract of Children*

Nose	Mouth breathing Nasal voice Cough
Pharynx	Dysphagia "Thick" voice Breathing obstruction in certain positions
Trachea	Dyspnea (chiefly inspiratory) Wheezing Brassy cough Inspiratory indrawing of suprasternal area and intercostal spaces
Larynx	Hoarseness or aphonia Dyspnea (chiefly inspiratory) Dysphagia Croupy cough Stridor Inspiratory indrawing of suprasternal area and intercostal spaces Restlessness
Bronchi	Dyspnea Wheezing Cough Evidence of collapse of portion of lung Obstructive emphysema Interstitial emphysema No respiratory tract signs

From G. B. Logan: The Diagnosis of Obstructive Lesions of the Respiratory Tract of Children. Proc. Staff Meet., Mayo Clin., Vol. 25.

Dyspnea which is encountered among children who have obstructive lesions in the larynx is usually inspiratory. It is manifested by the retraction of the suprasternal region, the intercostal spaces and also the epigastric region. Dyspnea of children who have obstructive lesions in the trachea is also usually inspiratory. The nature and the location of the lesion in the tracheobronchial tree may modify the type of dyspnea. Among children who suffer from asthma the dyspnea is chiefly expiratory.

Nasal, Pharyngeal Obstruction

Seldom does disease of the nose or pharynx cause such acute breathing trouble that it must be dealt with in emergency fashion. Crusting of the nose, however, in tiny infants may cause considerable dyspnea. Removal of the crusts promptly relieves the patient.

Laryngeal and Tracheal Obstruction

When the obstruction is thought to be in the larynx or trachea, the immediate question to be answered is whether the child's airway is sufficiently compromised to warrant the insertion of a tracheotomy tube. It is well known, though sometimes forgotten, that tracheotomy will give relief to children having obstruction at or above the subglottic area only, that is, above the point of the inserted tube. If, when first seen, the child is markedly dyspneic, is hoarse or aphonic, has stridor and inspira-

tory indrawing of the suprasternal, supraclavicular and intercostal spaces, tracheotomy is indicated as an emergency procedure. This is also the case if the child's inspiratory indrawing increases during a short period of observation and if the child displays increasing restlessness. The indications for tracheotomy otherwise will vary a little, depending on the disease and the individual situation. Further comments on this point are included in the sections on Acute Laryngotracheobronchitis and on pulmonary complications of poliomyelitis. Let us consider briefly the diagnosis and management of diseases of this region which require urgent treatment.

Croup. Spasmodic croup is one of the commonest causes of inspiratory difficulty in young children. The onset is usually sudden and usually at night after the patient has been asleep for a time. However, symptoms may appear in the daytime. Croup may be preceded by an apparently mild infection of the respiratory tract. A harsh, brassy cough and inspiratory stridor are the initial symptoms. Some or all of the symptoms of laryngeal obstruction are usually present. The voice becomes hoarse or disappears. Fever is rarely present. The symptoms, especially in young children, become progressively worse, but after several hours they generally subside spontaneously. Relief may be obtained in a short time, however, by the simultaneous use of inhalations of moist air and oral administration of antipyrine.

A steam kettle may be the only method of increasing moisture in the home. Its use introduces a hazard of burning the patient or siblings who are runabouts. Devices for producing steam may also make the patient's room excessively hot. The so-called cold steam devices are preferable if they can be obtained.

An atmosphere high in moisture content may be temporarily produced by allowing a hot shower to run for a few minutes in a bathroom with the door closed.

Approximately 1 grain (0.065 gm.) of antipyrine for each year of the child's age, to the age of three years, is a safe and effective dose. This may be repeated in an hour and at four-hour intervals thereafter, if necessary, for four or five doses. A teaspoonful of syrup of ipecac as an emetic is sometimes useful if the need for relief seems more urgent or if the moist air inhalations fail to bring prompt relief. Rest in bed in a room in which the atmosphere is warm and moist is advisable for a day or two after the initial attack, since sometimes the difficulty recurs on one or more successive nights. Tracheotomy is practically never necessary.

Acute Laryngotracheobronchitis. If the symptoms of croup are not alleviated after a few hours of treatment, the probability that they may be caused by acute laryngotracheobronchitis should be considered seriously. If this condition is present, the dyspnea will persist or become

progressively severer. Fever and evidence of marked toxicity often appear early, especially among infants. The borderline between croup and acute laryngotracheobronchitis is not always easily drawn.

Children having acute laryngotracheobronchitis are best treated in a hospital where apparatus to provide therapeutic high humidity are available and facilities for tracheotomy or bronchoscopy are present.

High moisture content of the inspired air is essential. All apparatus for the production of high moisture content have some disadvantages. The dangers of the use of a steam tent or steam room have been mentioned, though their use may be the only means of assuring the patient air of high humidity. Oxygen should be well moistened if administered, since unmoistened oxygen exerts an undesirable drying effect on the secretions of the respiratory tract. My colleagues and I have found the Mist-O_2-Gen tent and generator most satisfactory for this purpose. The croupette oxygen and humidity tent is also of value, though an accessory nebulizer is required if any medication other than a wetting agent is to be nebulized.

Various adaptations of the vaponephrin or DeVilbiss number 40 nebulizers have been described.[16] Sometimes more than one unit may have to be used.

Any apparatus must be checked at least every half-hour while in use. If a nebulizing unit is not working well, it must be cleaned immediately or a clean unit substituted.

It is most important to remember that extremely high humidity is necessary.

Moisture particles are said to be rendered smaller if a 2.5 to 5 per cent solution of propylene glycol is used instead of distilled water. The moisture cloud is suspended better if a 2.5 per cent solution of glycerin is used. The two solutions may be combined. The use of wetting agents in the nebulized solution was suggested a few years ago.[11, 15] A commercially available preparation (Alevaire) incorporating one of these substances (triton WR-1339) has been used widely in the past two years. In some instances we have had the impression that its use has been more helpful than moisture alone. It has been impossible, however, to conduct any well controlled observations. One recent study[18] suggests that Alevaire has no more value in the treatment of atelectasis of the newborn than does oxygen alone. Alevaire contains sodium bicarbonate. Its prolonged administration might cause alkalosis in small infants.

Antibiotic agents may be incorporated into the solution to be nebulized when the patient is known to have or is suspected of having an infection due to an organism susceptible to penicillin or streptomycin. Penicillin is used in a concentration of 5000 units per milliliter of solution. Customarily, the daily dose of streptomycin (40 mg. per kilogram

of body weight per twenty-four hours) is administered in the quantity of solution to be nebulized.

If the child is able to take fluids by mouth, the use of a saturated solution of sodium or potassium iodide is worth while as an additional means of keeping the secretions of the respiratory tract as fluid as possible. Five drops three times daily generally can be given to a child two years of age.

The fluid intake of the patient must be kept at an adequate level. If fluids cannot be taken by mouth, they should be given by the intravenous or subcutaneous route.

An effort always should be made to culture secretions from the tracheobronchial tree. Secretions from the pharynx or nasopharynx may be all that can be secured for culture. Whenever tracheotomy is done, bacteriologic examination of the tracheal secretions should be made.

The choice of antibiotic agent depends, of course, on the infecting organisms. Acute laryngotracheobronchitis is a disease which may be caused by various bacteria and possibly, at times, by a virus. Hemolytic streptococci, *Streptococcus viridans, Micrococcus pyogenes,* various pneumococci and *Hemophilus influenzae* have been known to be causative agents. The last agent may produce a severer disease and often causes supraglottic rather than subglottic edema. Initially, we prefer to use penicillin (300,000 units of aqueous procaine salt daily) and streptomycin (40 mg. per kilogram of body weight daily divided into two doses) by the intramuscular route. It is advantageous to administer medicaments by the parenteral route to very sick infants. Terramycin may be given intramuscularly (40 mg. per kilogram of body weight divided into three doses given every eight hours) or intravenously (40 mg. per kilogram of body weight slowly throughout the twenty-four hour period). A similar dose of tetracycline hydrochloride (Achromycin hydrochloride) may be administered in like manner.

The use of atropine is contraindicated. Sedative drugs and morphine are also contraindicated because their use obscures the indications for tracheotomy. Their use in the tracheotomized patient may obscure the signs of obstruction in the tube or in the air passage distal to the tube.

Occasionally, allergic edema of the tracheobronchial tree may be encountered accompanying acute infectious laryngotracheobronchitis.[8] Under such circumstances the subcutaneous administration of an aqueous solution of 1:1000 epinephrine is helpful. The use of antihistaminic drugs has been suggested. In my opinion, their drying action plus their sometimes sedative effect contraindicates their use.

If the patient's airway becomes more compromised in spite of adequate treatment with humidity and antibiotics, tracheotomy is indicated. This is clinically evident by increasing restlessness and increasing

inspiratory indrawing of the suprasternal, supraclavicular and intercostal spaces.

Tracheotomy is best done when an airway or small bronchoscope is in place. We prefer the use of a bronchoscope. Under such circumstances the operation may be done in an unhurried manner. The use of direct laryngoscopy on a child suspected of having acute laryngotracheobronchitis is not wise unless one is prepared to perform tracheotomy immediately.

If tracheotomy becomes necessary, it is essential that the child be replaced promptly in the moist oxygen tent after operation and that he be provided with air or oxygen of high moisture content until the tube can be removed.

Capillary Bronchitis (Acute Bronchiolitis, Acute Terminal Bronchitis). This condition, encountered chiefly among infants less than one year of age, is managed in much the same way as is acute laryngotracheobronchitis except that tracheotomy is valueless. The disease is so named because of the apparent predominant involvement of the terminal bronchioles. The infant appears to be gravely ill, has a frequent distressing cough, usually a fever of more than 102° F., rapid respirations and marked to severe dyspnea. Auscultation reveals many fine rales in part or all of the lungs. This condition may be associated with acute laryngotracheobronchitis. Almost invariably evidence of bronchopneumonia is present in small regions of the lungs.

Diphtheria. While diphtheria is now a rather uncommon disease in the United States, laryngeal diphtheria as a cause of inspiratory difficulty must always be considered. If diphtheria involving the nose or throat has been diagnosed, laryngeal complication should be expected. In many instances the first sign of diphtheria is croup which frequently occurs in the daytime. The dyspnea is progressive, and the nocturnal croupiness does not subside. The voice becomes hoarse, and the child often becomes aphonic. The previously described signs of laryngeal obstruction appear. As the condition progresses, expiratory difficulty also may be noted. In all cases in which diphtheria is suspected, swabbings of the throat should be cultured on appropriate media. In many instances of laryngeal or tracheal diphtheria, cultures may fail to reveal *Corynebacterium diphtheriae*. If the presence of diphtheritic infection is suspected, diphtheria antitoxin should be administered without waiting for the results of the cultures.

The same general plan of treatment as previously outlined for laryngotracheobronchitis, except for the use of antibiotics, may be used in the treatment of patients who have laryngeal diphtheria. However, diphtheria antitoxin should be administered as early as possible. If the disease is mild or moderately severe, 20,000 to 40,000 units of

antitoxin should be given. If the patient is seriously ill, 40,000 to 80,000 units should be administered. The intramuscular route is preferable, but if the child is extremely ill, the serum should be administered intravenously. It is always wise to give what may appear to be an unnecessarily large dose rather than give a dose that may be inadequate. One large dose of antitoxin given early in the course of the disease should suffice, but it may be repeated in several hours if necessary. Needless to say, sensitivity to the serum to be used should be determined by preliminary skin test or by the ophthalmic test. If the results of these tests are positive, the usual precautions must be observed to prevent severe or serious reaction. Erythromycin is effective against *C. diphtheriae*. It may be given orally or intravenously. Orally the daily dose is 20 to 25 mg. per kilogram of body weight divided into four doses given every six hours. Intravenously the dose is about 15 mg. per kilogram of body weight divided into four doses and given every six hours.[14]

BRONCHIAL OBSTRUCTION

The two most important causes of bronchial obstruction which have to be treated on an emergency basis are (1) foreign bodies and (2) asthma. Only the emergency treatment of asthma will be discussed here.

Asthma

The dyspnea of asthma is chiefly expiratory, though in some small infants inspiration may be equally affected. The dyspnea is almost always accompanied by marked wheezing.

The best drug for the immediate relief of an asthmatic attack is epinephrine. An aqueous solution of 1:1000 is administered subcutaneously. It is rarely necessary to give a child a dose greater than 0.5 cc. Several small doses administered at intervals are more effective and better tolerated than a single large dose. The drug also may be administered in peanut oil or in a gelatin mixture, the dose being the same as that of the aqueous solution. Theoretically, the advantages of the peanut oil or gelatin preparation are slowness of absorption and relatively prolonged action. The oil preparation, however, often fails to exhibit these advantages; furthermore, the oil itself occasionally causes allergic reactions.

Epinephrine also may be administered in a 1:1000 solution by means of a nebulizer. A few drops of the solution are placed in the all-glass or plastic nebulizer, the nozzle is directed down the patient's throat, and the bulb is squeezed as the patient inspires. One or two squeezes

during each of three to five inspirations will generally suffice. For small children the nebulizer can be operated by an adult; older children learn easily to use it themselves. Untoward reactions to epinephrine are rarely seen even when the drug is used repeatedly in this manner.

Isopropylepinephrine (Aleudrin, Isuprel, Norisodrine) also may be used in this same way. Isuprel is available for this purpose in a 1:200 solution, and Norisodrine may be obtained in 10 and 25 per cent powder preparations for use in a special inhaler.

Ephedrine hydrochloride or sulfate, which is given in capsule form by mouth, is often effective in controlling asthmatic attacks. It may be given to small children as a powder in syrup or jelly. The dose for older children is ⅜ grain (0.024 gm.); for younger children, 3/16 grain (0.012 gm.) or less may be effective. One-half to ¾ grain (0.032 to 0.05 gm.) of one of the barbiturates is administered concomitantly to combat the stimulating effect of the ephedrine as well as to calm the patient.

Aminophylline may be used orally, rectally or intravenously. It is of value for patients who do not react favorably to epinephrine. Some authors consider aminophylline more useful in a prolonged attack of bronchial obstruction than in an acute attack. I have found that it may be of value in both conditions. Several commercial preparations of the drug which are designed for oral use are available in either the pure form or combined with a barbiturate and ephedrine.

Suppositories of aminophylline combined with one of the barbiturates in a cocoa butter base are frequently useful. Children who are sensitive to chocolate should not be given this preparation. The action of the drug, when it is administered rectally, is slower but somewhat more prolonged than when given orally or intravenously. Aminophylline, 3¾ grains (0.25 gm.), together with Seconal sodium (sodium propylmethylcarbinylallylbarbiturate) or pentobarbital sodium, ¾ grain (0.05 gm.), may be given in this manner to children two to ten years of age. Older children may require 5 to 7 grains (0.3 to 0.45 gm.) of aminophylline. The drug also may be given in solution by rectal instillation. This mode of administration produces rectal irritation in some cases.

The intravenous administration of aminophylline produces a prompter effect than oral or rectal administration; however, it is important that it be given slowly. The dose for a ten-year old child is 3¾ grains (0.25 gm.); about half this dose is given to small children. Aminophylline, when given intravenously, often is combined with glucose. Patients who have severe asthmatic attacks benefit from the intravenous administration of 100 to 300 cc. of a 25 per cent solution of glucose. Larger amounts of a 10 per cent solution often are effective.

Oxygen administered by means of a tent or mask is sometimes help-

ful. The combination of 80 per cent oxygen and 20 per cent helium is frequently very effective. Since this mixture is given best by mask, its use, unfortunately, is limited to those children who will tolerate a mask and for whom a small-sized mask can be secured. The use of a tent for the administration of such an oxygen-helium mixture is not completely successful unless the tent is practically airtight.

Many small children have attacks of asthma associated with or accompanying infection of the respiratory tract. The prompt administration of an appropriate antibiotic drug should be started at the time the initial dose of epinephrine is given. If the antibiotic drug administered is penicillin, its use should be continued for at least five days after temperature of the child has become normal; if sulfonamides or the so-called broad-spectrum antibiotics are given, administrations should be continued for forty-eight hours after the temperature has become normal.

In infants and small children having asthma the thick bronchial secretions are the main pathologic condition to be combated. The prompt and continued use of air or oxygen of high humidity is important; in some cases it is lifesaving. The concomitant administration of iodides is also wise. Their effect is not always noted at once. A suggested dosage is 5 drops three times daily of a saturated solution of potassium iodide for a two-year old child.

For patients who have *status asthmaticus* the rectal administration of ether in oil is a useful procedure. Three to 4 ounces of ether mixed with an equal amount of warmed olive oil are instilled through a small rubber catheter. An amount smaller than the initial dose may have to be repeated at intervals of a few hours for twenty-four hours.

Corticotropin (ACTH), cortisone and hydrocortisone recently have been added to our therapeutic armamentarium. They are useful drugs for treating patients who no longer respond to epinephrine or aminophylline. *They should not be used when other drugs will give relief.* The dosage schedule suggested in Table 6 may be followed when necessary.

PNEUMONIA

Pneumonic processes may produce dyspnea which is not attributable to obstruction. The cause seems to be a combination of pain, toxicity and reduced vital capacity. Space does not permit detailed discussion of the different types of pneumonia.

The onset of primary pneumonia is characterized by fever, dyspnea and cough. Various types of pneumococci are etiologic agents. The child's face is flushed, the alae nasi dilate with each inspiration, and the respiratory rate is increased. This chain of events generally follows

TABLE 6. *Suggestions for Administration of Corticotropin (ACTH), Cortisone and Hydrocortisone to Children Having Severe Asthma*

DAY OF TREATMENT	DOSE OF CORTICOTROPIN* (UNITS) BY AGE OF PATIENT			DOSE OF CORTISONE† (MG.) BY AGE OF PATIENT			DOSE OF HYDROCORTISONE‡ (MG.) BY AGE OF PATIENT		
	4 Years	10 Years	Adult	4 Years	10 Years	Adult	4 Years	10 Years	Adult
1	40	60	80	75	150	300	60	120	240
2	40	60	80	50	125	200	40	100	160
3	20	30	40	50	125	200	40	100	160
4	20	30	40	25	75	100	20	60	80
5	10	15	20	25	75	100	20	60	80
6	10	15	20	25	75	100	20	60	80
7				25	75	100	20	60	80
8				12.5	50	75	10	40	60
9				6.25	50	75	5	40	60

* Daily dose of corticotropin given intramuscularly in 4 divided doses every 6 hours.

† Daily dose of cortisone given intramuscularly in 1 dose.

‡ Smaller doses may suffice; some adults require only 80–100 mg. daily. Daily dose of hydrocortisone given intramuscularly in 4 divided doses every 6 hours.

a mild infection of the upper part of the respiratory tract. Children between the ages of about two and fourteen years who suffer from this type of pneumonia generally make a satisfactory recovery. In our experience this disease is now uncommon.

The use of sulfonamide and antibiotic drugs has lowered the mortality rate and has decreased morbidity.

Pneumonia due to organisms other than pneumococci seems to occur more frequently at the present time. Some of the organisms which seem to be of etiologic importance are hemolytic streptococcus, *M. pyogenes* (some strains resistant to penicillin and the tetracycline group of antibiotics), *H. influenzae* and viruses. The etiologic role of the bacteria mentioned may be proved by isolating the organisms from the blood, sputum or nasopharyngeal secretions. A viral etiology is often assumed when pathogenic bacteria are not obtained on culture, when the number of leukocytes in the patient's blood is normal or below normal, and when there is evidence on physical or roentgen examination of a patchy type of involvement of the lungs.

For initial treatment, penicillin administered intramuscularly is the drug of choice. If the etiologic organism is suspected to be other than pneumococcic or streptococcic, streptomycin should be administered concomitantly. An accurate choice of antibiotic or chemotherapeutic drug can be made when the infecting organism has been identified.

Increasing restlessness and dyspnea in the child are indications for the use of oxygen. The occurrence of cyanosis is also an indication, though it is wiser not to wait until it occurs before treatment with oxygen is started. A daily enema may be necessary in the early part of the disease to combat distention. Codeine in small doses is useful in some instances to control excessive coughing and to promote better rest.

SUDDEN DEATH

Occasionally the physician is confronted with the problem of an infant (usually two to six months of age) who has been found dead in bed. Although such infants are beyond help, the physician has the responsibility of bringing comfort to the parents. It is important, under such circumstances, to know and not to guess at the cause of death. The Conference on Sudden Death in Infants held on November 30, 1949, by the Federal Security Agency and the Public Health Service summarizes the problem as follows: "The first step in the solution . . . will be made when it is recognized that such certifications as accidental mechanical suffocation, status thymicolymphaticus, or aspiration of stomach contents in infants found dead or dying unexpectedly are usually erroneous. Infants found dead while in apparent health, show-

ing at autopsy insufficient gross findings to explain death, will as a rule show significant microscopic lesions that indicate the presence of fulminating disease. The practically uniform involvement of the respiratory tract suggests this as a portal of entry for the causative agent in most instances. The presence of profound vascular engorgement and of widespread parenchymal changes, degenerative and infiltrative that could very well represent the effects of vascular injury, speaks for systemic disease rather than rapidly acting violence as the usual cause of death."[1]

We have had such experiences with infants being found dead in bed. Necropsy has invariably disclosed evidence of pneumonia.

TRACHEO-ESOPHAGEAL FISTULA

This congenital anomaly must be promptly recognized, since early surgical correction is possible. The diagnosis usually is not made until the newborn infant is offered a feeding.[12] Three things should make one suspicious of its presence before a feeding has been given: (1) a noisy, gurgling type of respiration; (2) a continuous "spilling out" type of vomiting; and (3) a clear mucous type of vomitus. The diagnosis is confirmed by attempting to pass a small gavage tube, usually a number 10 French catheter. If obstruction is encountered, the infant should be examined roentgenologically. The site of the distal end of the tube should be determined. A small amount (½ to 1 teaspoon) of radiopaque substance, such as Umbrathor or sodium iodomethamate (Neoiopax), in a 35 per cent solution, may be used. Do *not* use barium.

Once the diagnosis is established, nothing further should be offered by mouth. Surgical correction should be prompt, but time may be taken to prepare the patient so that his condition is as good as possible. The urgency of the situation is not so great as to preclude the loss of a few hours for this purpose.

RESPIRATORY PROBLEMS ASSOCIATED WITH POLIOMYELITIS

Respiratory problems among patients suffering from poliomyelitis are encountered chiefly among those who are affected with the bulbar type. Pooling of secretion in the throat, nasal speech, hoarseness, inability to talk, stupor, stridor, dyspnea, cyanosis, variations in depth and rate of respirations, periods of apnea, anxiety and restlessness may be encountered singly or completely. Careful withdrawal of secretions by suction, the administration of moistened oxygen and the use of a respirator may be adequate in some instances to control these complications. Tracheotomy as originally advocated by Galloway[9] has been rather widely used in the past eight years as an additional means

of treatment. In our experience it has been a life-saving operation when proper indications necessitated its use. We agree with Priest and his co-workers[17] that tracheotomy should be done early when needed and that moistened oxygen should be administered via the tracheotomy tube. While there are no hard and fast indications for the operation, it should be done when other methods of clearing the airway of obstructive secretions have failed. *A child having bulbar poliomyelitis should be carefully watched, and, if symptoms of respiratory distress appear, tracheotomy should not be delayed.*

PNEUMOTHORAX

This condition is not commonly encountered among children. It may occur in the neonatal period either associated or unassociated with birth trauma. It also may occur among older infants as a complication of pneumonia, as the result of trauma or for no apparent reason. The degree of dyspnea is usually directly proportional to the amount of air in the pleural cavity and to the extent of displacement of the mediastinum. The diagnosis is made by determining that breath sounds are absent over part or all of one side of the thorax, by finding tympany to percussion in this region and by finding the heart and mediastinal structures shifted away from the side on which the air is located. Roentgen study of the thorax should be carried out to confirm the diagnosis. If symptoms are minimal, it is best to observe the youngster. Oxygen should be administered if cyanosis is present. If the intensity of the symptoms is moderate to severe, the air should be aspirated. If it is severe, air may be withdrawn by syringe and needle followed by constant drainage. Otherwise, a small S-shaped needle should be inserted without preliminary aspiration into the pleural space and gentle suction used to maintain a negative pressure. Appropriate antibiotic or chemotherapeutic drugs should be used if infection has preceded or is associated with pneumothorax.

ASPHYXIAL STATES

Accidental asphyxia is an acute emergency. In all instances, measures for the restoration of respiration must be instituted promptly by someone at the scene of the accident if the outcome is to be favorable.

Children who are apneic for fifteen minutes before artificial respiration is begun have a small chance for recovery, whereas there is a good chance for recovery when the apnea has been present only four to six minutes.[4] Children who have been asphyxiated by the inhalation of noxious gases, by drowning or by electric shock usually have to be treated by artificial respiration.

Artificial Respiration

After the child has been removed from the noxious gas, the water or the electrical contact, artificial respiration may be given by one of several methods. The arm lift-back pressure method has been shown recently to be superior to the prone pressure method of Schafer[10] and has the advantage over the Silvester method of having the patient in the prone position. If the rescuer (layman or physician) is familiar only with the Schafer method, it should be used. Since 1951 the American Red Cross and other agencies which teach first aid have been teaching the arm lift-back pressure method as the one of choice. The hip lift-back pressure method produces the largest volume of tidal air. It has the disadvantage of fatiguing the operator more quickly than do the other methods when the patient is an adult. When the patient is a small child, this method is advantageous.

The *arm lift-back pressure method* (Holger-Nielsen method) can be described briefly as follows:[2] "The subject is placed prone, elbows bent, arms overhead with one hand upon the other. The cheek is placed on the hand, the face turned slightly to one side. The operator kneels on one knee at the head of the subject and puts the foot of the opposite leg near the elbow. He places his hands on the subject's back, in such a way that the thumbs just touch, the heels of the hands being just below a line running between the armpits. He rocks slowly forward, elbows straight, until his arms are approximately vertical, exerting steady pressure upon the chest. Then he commences to rock backward slowly and slides his hands to the subject's arms just above the elbows. He raises the arms until resistance and tension are felt at the subject's shoulders. Then he drops the arms. This completes a full cycle. The cycles are repeated 12 times per minute, the expansion and compression phases being of equal length, the release periods being of minimum duration."

The *hip lift-back pressure method* is performed as follows:[10] The patient is placed in the prone position as for the Schafer method. The operator kneels on one knee at the level of the hip, straddles the patient and places the other foot near the opposite hip. He places his hands under the hips (at the anterior superior iliac spines) and raises the pelvis vertically 4 to 6 inches. The hips are then replaced on the ground and the operator shifts his hands to the patient's midback just below the scapulas with the fingers spread and the thumbs about an inch from the spinal column. He presses downward, then releases the pressure. As he lifts the hips he rocks backward, and as he exerts back pressure he rocks forward. In each phase he keeps his arms straight, so that the work of lifting and pressing is distributed over the shoulders and back, rather than being imposed primarily on the

arms. Active inspiration results from lifting the hips and active expiration from pressure on the midback. The full cycle of hip lift and back pressure is repeated twelve times per minute.

Artificial respiration often must be continued for several hours. The *Eve rocking device*[6, 13] not only is very suitable for this purpose, but also has some physiologic advantages to the patient over the manual methods. The device resembles a playground seesaw with the board wide enough to hold the child adequately. The child must be laid on the board face down and held on it securely by binding the ankles and wrists to the board or by some other method. The patient, with his abdomen over the fulcrum, is rocked through 45 degrees with a head-up and head-down position comprising one cycle. The cycle is repeated twelve to fifteen times per minute.[5] In his original article Eve[6] reported the use of a rocking chair as the rocking device for a two-year old child. A recent manual modification of this which is useful in treating small children has been described by Eve.[7] The method requires two operators who stand facing each other joining hands. The child is laid face down on the two pairs of arms. The operators tilt the body 45 degrees each way alternately twelve to fifteen times per minute.

The administration of oxygen during the period of artificial respiration is often of advantage. The use of a carbon dioxide-oxygen mixture does not seem of advantage, since apneic patients are hypercapneic. Some physicians advise the intravenous use of caffeine.

A mechanical resuscitator is useful only if the operator knows how to use the device. The Council on Physical Medicine and Rehabilitation of the American Medical Association[3] requires that any such device produce an inflationary pressure no higher than 20 mm. of mercury and no fewer than 10 cycles per minute if operating automatically on a volume of 500 cc. of air per cycle. Those which exert an alternating negative and positive phase should have a negative phase not exceeding 9 mm. of mercury. The total positive pressure variation should not be less than 8 mm. nor more than 20 mm. of mercury. For further listing of the minimal requirements of a resuscitator or inhalator the report of the Council should be read.

Additional Suggestions for Care of Asphyxiated Children

Children who have been asphyxiated with carbon monoxide should be given oxygen in as high concentration as possible during the resuscitation period. Methylene blue does not seem to be of as much value as it was once thought to be. Spinal puncture is occasionally of value to relieve complicating increased edema of the brain and increased intracranial pressure.

After resuscitation the patient should be kept warm and in bed and under close observation, in a hospital if possible, for two to three days. Antibiotic drugs such as penicillin and streptomycin should be given to combat any infection present or as a prophylactic measure. Fluids and food should be given as soon as tolerated and the amounts slowly increased as the patient is able to increase his intake.

REFERENCES

1. Adams, J. M.: The Pneumonias, in McQuarrie, I., ed.: Brennemann's Practice of Pediatrics. Hagerstown, Md., W. F. Prior Company, 1951, Vol. 2, Chap. 48, p. 30.
2. Council on Physical Medicine and Rehabilitation: Back Pressure-Arm Lift Method for Administering Artificial Respiration Recommended. J.A.M.A., *147*:1454, 1951.
3. Council on Physical Medicine and Rehabilitation: Tentative Minimal Requirements for Acceptance of Resuscitators and Inhalators. J.A.M.A., *150*:695, 1952.
4. DeSanctis, A. G., and Varga, C.: Handbook of Pediatric Emergencies. St. Louis, C. V. Mosby Company, 1951, p. 104.
5. DeSanctis, A. G., and Varga, C.: Op. cit., p. 112.
6. Eve, F. C.: Actuation of the Inert Diaphragm by a Gravity Method. Lancet, 2: 995, 1932.
7. Eve, F. C.: Artificial Circulation Produced by Rocking: Its Use in Drowning and Anaesthetic Emergencies. Brit. M. J., 2:295, 1947.
8. Everett, A. R.: The Problem of Acute Laryngotracheobronchitis. Eye, Ear, Nose & Throat Monthly, 32:142, 1953.
9. Galloway, T. C.: Tracheotomy in Bulbar Poliomyeltis. J.A.M.A., *123*:1096, 1943.
10. Gordon, A. S., Sadove, M. S., Raymon, F., and Ivy, A. C.: Critical Survey of Manual Artificial Respiration. J.A.M.A., *147*:1444, 1951.
11. Hall, G. C.: Pulmonary Toxicity of Wetting Agents Dispensed as Aerosols. Am. J. Dis. Child., 80:408, 1950.
12. Harris, L. E.: Emergencies in the Newborn Period. Minnesota Med., 33:1204, 1950.
13. Lahiff, J. R.: Rocking Device for Artificial Respiration. Brit. M. J., 2:42, 1943.
14. Martin, W. J., Nichols, D. R., and Geraci, J. E.: The Present Status of Erythromycin. Proc. Staff Meet., Mayo Clin., 28:609, 1953.
15. Miller, J. B., Abramson, H. A., and Ratner, B.: Aerosol Streptomycin Treatment of Advanced Pulmonary Tuberculosis in Children. Am. J. Dis. Child., 80:207, 1950.
16. Miller, J. B.: Apparatus for Prolonged Continuous Aerosol Administration. Am. J. Dis. Child., 84:616, 1952.
17. Priest, R. E., Bois, L. R., Goltz, N. F., Younger, L. I., and Koller, R. L.: The Present Status of Tracheotomy in Bulbar Poliomyelitis. Ann. Otol., Rhin. & Laryng., 60:468, 1951.
18. Silverman, W. A., and Andersen, H. H.: A Controlled Study of the Influence of Triton WR-1339 Aerosol upon Death Rate and Incidence of Hyaline Membrane Disease among Premature Infants. Read at the meeting of the Society for Pediatric Research, Buck Hill Falls, Pa., May 5, 1954.

Mayo Clinic
Rochester, Minnesota

FOREIGN BODIES IN THE AIR AND FOOD PASSAGES

PAUL H. HOLINGER, M.D.

KENNETH C. JOHNSTON, M.D.

The aspiration or ingestion of a foreign body is a common accident that befalls children and adults alike. The frequently encountered peanuts, pennies and safety pins found in the air and food passages of children are matched or surpassed in frequency by the fish, chicken and steak bones and the parts of dental bridges or plates found in the esophagus or bronchi of adults. An analysis of cases indicates that these accidents are common, permitting an evaluation of a series of sufficient size that conclusions regarding etiology, diagnosis and treatment are of statistical significance.

ETIOLOGY

The age distribution of various foreign bodies shows an interesting pattern. Data concerning 2042 cases of foreign bodies in the air and food passages are tabulated, and reference to the tables demonstrates that while patients of any age (two days to ninety-two years) may swallow or aspirate a foreign body (Fig. 4), certain objects (Table 10) are found most frequently in specific age groups. Thus safety pins as foreign bodies are found most frequently in children seven months to two years of age; peanuts in children fifteen months to four years of age; coins in children two to four years of age; hardware in children three to seven years of age; and chicken bones in adults thirty to seventy years of age. In the last group the bones are found almost invariably in the cervical esophagus, whereas in infants and children,

From the Department of Otolaryngology, University of Illinois College of Medicine, and the Children's Memorial and St. Luke's Hospitals, Chicago.

spicules of chicken bones are *aspirated* foreign bodies, located in a bronchus.

Certain recurring foreign bodies in infants and children deserve special mention. Until a child has molar teeth he should not be given nuts, nut-candies or nut cookies. These treacherous foreign bodies cannot be satisfactorily chewed, they initiate coughing when they reach the pharynx, and aspiration follows. Raw carrots and crisp bacon act in an identical manner, and yet these two items are often on the diet list of infants! The frequency with which they are seen as foreign bodies makes it appear that they should be removed from diet lists.

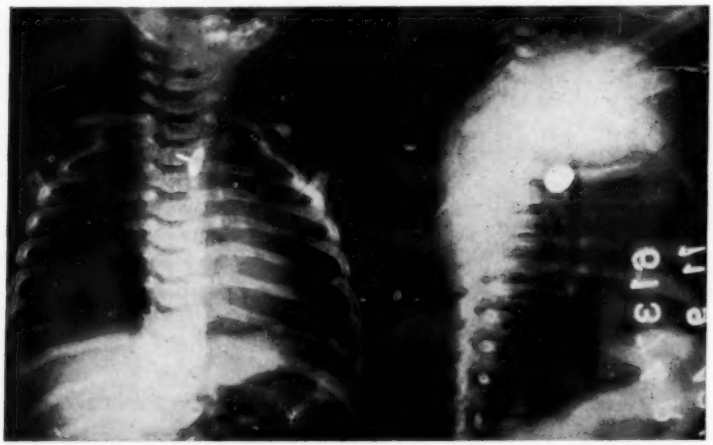

Fig. 4. Infant less than 1 month of age with a thumb-tack in the esophagus. It had been used to hold the lace in the hood of the bassinet and had fallen into the infant's open mouth as it was crying.

Other statistical data give the numbers of various types of foreign bodies found in the series (Table 7), the site at which each foreign body was found (Table 8), and other factors concerned with age incidence (Tables 9 and 10).

In seventy-six cases multiple foreign bodies were found. One infant who had acute respiratory obstruction had been chewing a string of beads; the string broke, and while many beads were swallowed, two were aspirated, one becoming lodged in each bronchus. Another child thought to have swallowed a penny actually had swallowed three cents, the pennies being superimposed on each other in the anteroposterior roentgenogram, but separately visualized in a true lateral view. In another instance a two and a half year old girl swallowed four open safety pins and two uniform buttons, one with a stud attached, which all became imbedded in the upper thoracic esophagus. Another case

TABLE 7. *Classification of Extracted Foreign Bodies in 2042 Consecutive Cases*

FOREIGN BODIES	TOTAL NUMBER	PERCENTAGE
Bones	390	18
Coins	291	14
Nuts	287	14
Hardware, metallic objects	280	13
Safety pins	242	12
Meat	210	10
Vegetable matter (other than nuts)	155	7
Dental objects	75	4
All others	169	8
Total	2099	100

TABLE 8. *Anatomic Location of Foreign Bodies in the Air and Food Passages*

ANATOMIC LOCATION	TOTAL NUMBER		PERCENTAGE
Vallecula	14		1
Hypopharynx	94		4
Larynx	34		2
Trachea	51		2
Bronchi:	640		30
Right bronchus		419	
Left bronchus		221	
Esophagus:	1209		57
Cervical esophagus		821	
Thoracic esophagus		257	
Cardiac esophagus		131	
Stomach and duodenum	75		4
Total	2117		100

TABLE 9. *Age Distribution of Foreign Bodies in 2042 Consecutive Cases*

AGE	TOTAL	PERCENTAGE
Under 1 year	215	10
1–2 years	363	18
2–4 years	494	25
4–14 years	284	14
Adults	686	33
Total	2042	100

TABLE 10. *Age Distribution of the Most Commonly Encountered Foreign Bodies*

AGE GROUPS	SAFETY PINS	NUTS	COINS	BONES AND MEAT
Under 1 year	106	6	20	4
1–2 years	71	108	62	14
2–4 years	31	130	140	17
4–14 years	7	34	63	19
Adults	27	9	6	546
Totals	242	287	291	600

of multiple foreign bodies was that of a sixteen year old boy who fell into a corn crib. When he was rescued, his mouth and nose were quickly cleared of corn kernels, but extreme dyspnea and wheezing persisted. Seven whole kernels of corn and a large piece of corn husk were removed from the trachea and both bronchi.

Specific etiologic factors may be noted from an analysis of the statistics. Chevalier Jackson has repeatedly demonstrated that carelessness is a constant etiologic factor. As an example, many infants swallow *open* safety pins which become lodged in the air or food passages, requiring

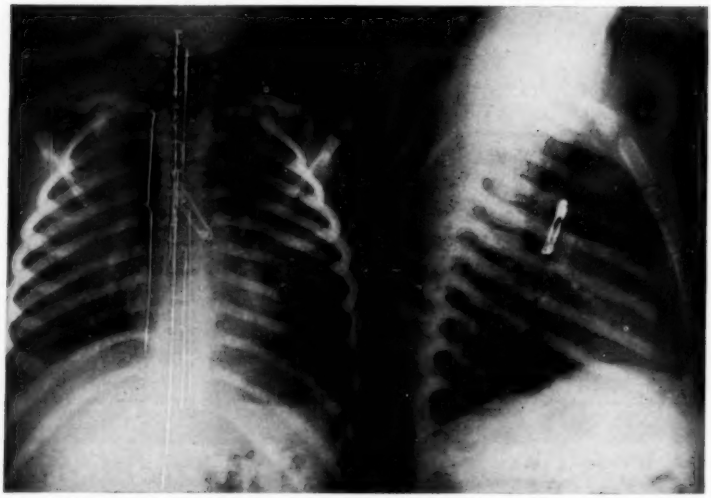

Fig. 5. Multiple foreign bodies, 2 *closed* safety pins, in the left main bronchus. The amount of air entering the left lung is not reduced, but the flow is disturbed to produce a wheeze, the first stage of bronchial obstruction.

removal. Only in the rare instances is it necessary to remove a *closed* safety pin, and then only because the pin is unusually long or lodges in a bronchus (Fig. 5). For example, one infant swallowed two large interlocked safety pins which were free in the stomach; it was felt that they were too long to pass through the turns of the duodenum, and they were removed endoscopically with fluoroscopic assistance.

General anesthesia and unconsciousness from other causes are etiologic factors, as in the aspiration of loose teeth during tonsillectomy (Fig. 6) or in an epileptic convulsion.

In many of the cases of esophageal foreign bodies a pathologic lesion of the esophagus produces a partial esophageal obstruction and is consequently a direct etiologic factor responsible for the lodgment of the foreign body. Not infrequently a foreign body accident is the first

indication to the patient that an esophageal lesion exists. Congenital esophageal stenosis, lye strictures and other benign stenoses of the esophagus are not infrequently first discovered in this manner. Often a careful history may suggest that the child had been considered a feeding problem before such obstruction finally revealed the true cause of the child's dysphagia.

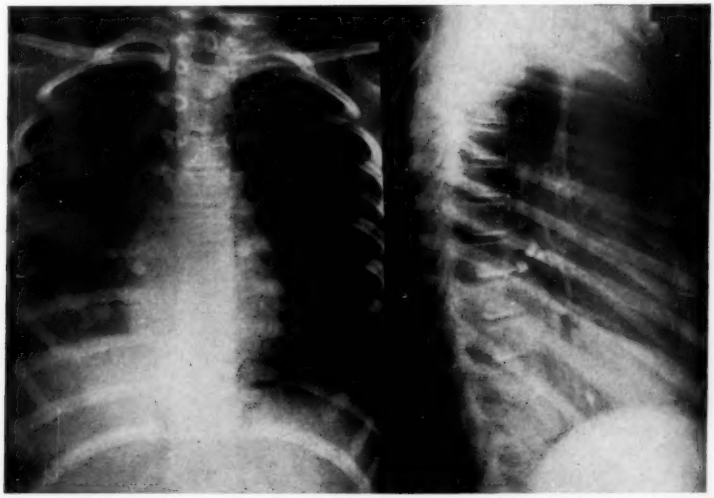

Fig. 6. Deciduous canine tooth aspirated during tonsillectomy. Complete obstruction of the basilar divisions of the right lower lobe has resulted in atelectasis of these segments with the characteristic triangular density, shift of the heart toward the involved side and elevation of the involved diaphragm.

A subnormal mentality or neurologic lesions influencing muscles of deglutition were likewise etiologic factors in several instances in children as well as adults. A mongol who had swallowed a large brooch and a postbulbar poliomyelitis patient who swallowed a small harmonica because of his muscular incoordination are examples of this group.

SYMPTOMS

Everyone has had the personal experience of the momentary lodgment of an unexpectedly large bolus of meat in the esophagus, or of choking on food which was inadvertently aspirated to cause severe coughing paroxysms. These symptoms are distressing and often alarming and may usually be elicited in the history of a foreign body accident if the patient is old enough to describe them (Fig. 7).

Careful analysis reveals that the general symptoms of foreign bodies

in the air and food passages may be divided into three stages. The *initial symptoms* consist in the violent paroxysms of coughing and gagging which occur as the foreign body is first swallowed or aspirated. This is generally followed by a *symptomless interval*, so designated because the foreign body becomes fixed in a bronchus or the esophagus and the immediate, irritating symptoms subside. This stage is most treacherous and accounts for a large percentage of cases of delayed diagnosis or completely overlooked foreign bodies. It is during this stage that one is inclined to minimize a foreign body history, taking false assurance from the fact that if the patient has no symptoms he either has no foreign body or it is in a position in which it will do no harm.

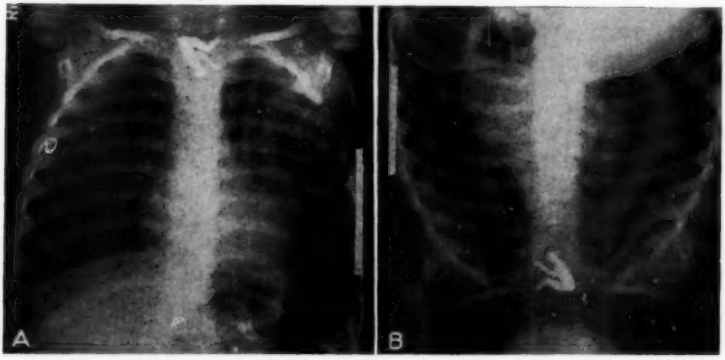

Fig. 7. Roentgenograms of a 2 year old boy who said he had swallowed a soldier. *A*, Upright chest film showing foreign body. *B*, Film inverted to demonstrate the machine-gunner sitting in the cervical esophagus.

A simple illustration of a child who has swallowed an open safety pin refutes such reasoning. The initial symptoms of choking and gagging are usually violent when the pin is in the hypopharynx (Fig. 8), but quickly subside as the pin reaches the thoracic esophagus (Fig. 9). Here it may remain fixed for several days, causing no symptoms as the infant swallows its liquid formula without evidence of obstruction. There may be no symptoms whatsoever until the point perforates the esophagus and penetrates the pleura, the aorta or even the heart.

This suggests the third stage of the symptomatology, the stage characterized by the *symptoms of complications:* that stage in which obstruction of the esophagus or bronchus, erosion or infection develops to direct attention again to the presence of the foreign body (Fig. 10).

Certain more specific symptoms are dependent on the location of the foreign body. Hoarseness, cough and dyspnea result if the object is in the larynx. These same symptoms, however, may be present if a

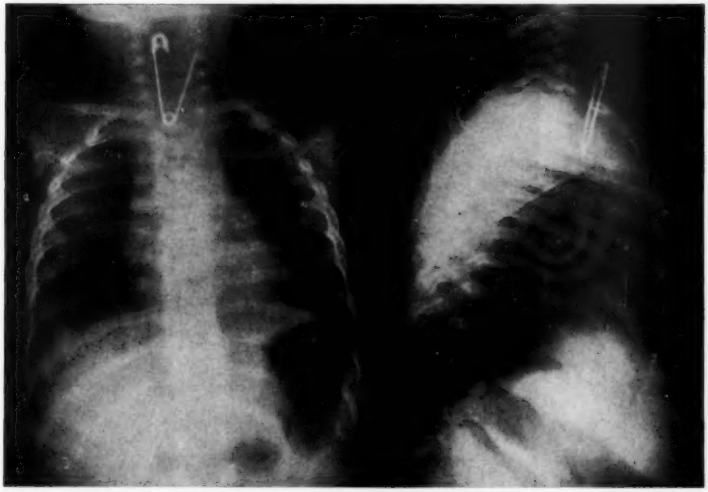

Fig. 8. Recently swallowed open safety pin in the cervical esophagus, where it produces violent initial symptoms of coughing, choking and gagging. Note that on the anterior-posterior view the pin is seen above the level of the clavicles, but that the lateral view shows all but the tip of the keeper to be lodged in the esophagus below the level of the arytenoids.

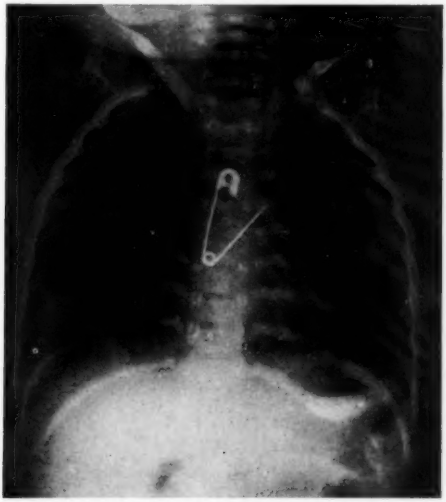

Fig. 9. Open safety pin in the thoracic esophagus. In this position the acute initial symptoms subside and there is a symptomless interval. The infant swallows without difficulty; consequently one may be inclined to minimize the foreign body history of the initial symptoms, resulting in a serious delay in diagnosis.

Fig. 10. Empyema resulting from perforation of the esophagus by an open safety pin. The initial symptoms had been forgotten when the infant had "pneumonia" 3 weeks later and was finally hospitalized because of the progressively severe pulmonary involvement. When the roentgenogram demonstrated the pin, the mother immediately recalled the date of the accident. Thus this stage of complications had been preceded by the initial symptoms and the symptomless interval.

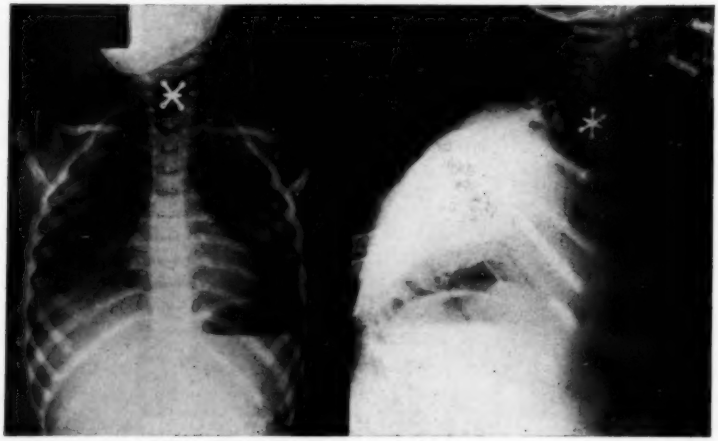

Fig. 11. Jackstone in the esophagus causing severe laryngeal symptoms of choking and dyspnea because of the overflow of saliva into the larynx and the tracheal compression.

large foreign body lodges in the cervical esophagus, producing tracheal compression and a flow-over of saliva into the larynx (Fig. 11). Foreign bodies in the trachea produce an extreme wheeze and dyspnea, giving bilateral pulmonary findings of obstruction. If the object is loose in the trachea, it rattles up and down with respiration, hitting the carina on inspiration and the larynx with a painful slap on the succeeding cough or expiration. In the bronchi the object may give the classical symptoms of an asthmatic wheeze (Fig. 5), obstructive emphysema (Fig. 12) or atelectasis (Fig. 6), dependent upon the degree of obstruction. In the esophagus the most constant symptom is difficulty

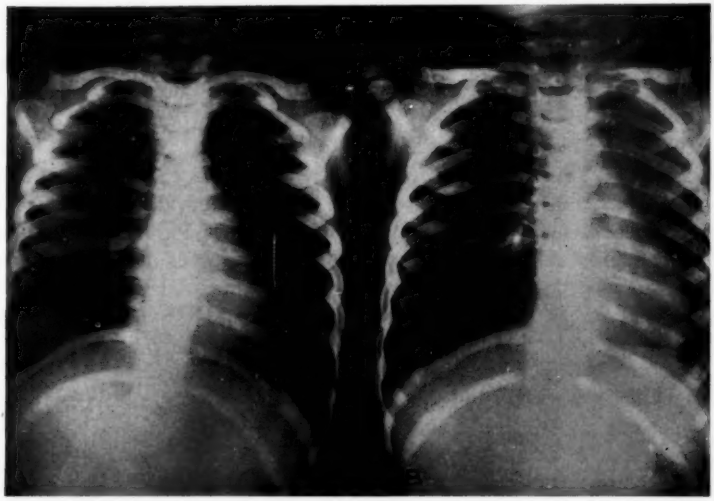

Fig. 12. Obstructive emphysema of the right lung due to a peanut in the right bronchus. *A*, Film on inspiration showing a normal chest. *B*, Film on expiration; air can leave the left lung, but is trapped in the right lung. The heart and mediastinum shift to the left on expiration, and the left diaphragm rises. The right diaphragm remains stationary.

in swallowing or the complete inability to swallow; in some cases pain on swallowing is second in importance only to dysphagia.

PATHOLOGY

Many factors determine the pathologic changes caused by foreign bodies. The type of foreign body, its location and sojourn, the age of the patient and previous attempts at removal indicate a few of the variables. Foreign bodies in the vallecula and hypopharynx cause such

severe distress that early diagnosis and prompt removal leave little opportunity for severe local injury.

CASE I. An example of a fatal complication in one such case occurred in an infant who had been unusually irritable for several days, having what appeared to be a respiratory infection with fever, croupy cough, restlessness and some regurgitation of feedings. After a sudden, severe oral hemorrhage, x-ray studies were made which revealed an open safety pin in the hypopharynx, point upward and spring downward in the cervical esophagus. Recovery appeared satisfactory after endoscopic removal, but 6 months later an aneurysm of the carotid artery developed which ultimately proved fatal.

Foreign bodies in the larynx of infants or children generally consist of sharp, flat objects such as eggshells and open safety pins, or occasionally a chicken bone or a watermelon seed. They produce laryngeal edema and hoarseness, and in rare instances it becomes necessary to tracheotomize the patient. Laryngeal edema and inflammation, as well as bronchial edema, follow the aspiration of such foreign bodies as peanuts and corn into the tracheobronchial tree. Some foreign bodies, such as a nail loose in the trachea, produce traumatic laryngeal edema as they strike the inferior surfaces of the cords on each expiration and cough. Generally such edema subsides after removal of the foreign body without further operative intervention.

The trauma due to foreign bodies in the bronchi is dependent upon the degree of bronchial obstruction they produce and the consequent pulmonary suppuration. The severest complications follow the aspiration of vegetable foreign bodies. Acute pneumonia or pneumonitis, atelectasis, drowned lung, obstructive emphysema, massive pulmonary hemorrhage, multiple lung abscess, empyema, bronchial stenosis and bronchiectasis are the principal pulmonary complications. Metallic foreign bodies produce less severe complications in general, but far advanced bronchiectasis or pulmonary hemorrhages may be responsible for the discovery of foreign bodies as roentgenograms reveal previously overlooked objects. Some may be present in the lung many years; in one case a wood screw was present thirty-five years, having been aspirated when the patient was four years of age. He was thought to have had whooping cough at that time, although it was known that he had had whooping cough in infancy.

Lobectomy is recommended in each case in which bronchiectasis has developed, but only after the foreign body has been removed and adequate drainage has resulted in a marked general improvement of the patient. In another case a metallic object produced a pneumothorax; a nail in the right lower lobe bronchus perforated the pleura prior to admission to the hospital. After removal of the foreign body the lung re-expanded without further complication. Extensive mediastinal, pericardial, cervical and subcutaneous emphysema developing over a period of forty-eight hours led to the discovery of a peanut in the right bronchus

of a four and a half year old girl. The emphysema subsided after removal of the foreign body, although the child had to be kept in oxygen for several days. Empyema may follow the aspiration of a grass head as the multiple sharp points on the grass head drive it into the pleural cavity by a ratchet-like action.

The many pathologic changes produced by foreign bodies in the esophagus are associated with obstruction, stenosis, erosion, ulceration or perforation of the esophagus. Relatively minor complications of esophagitis with small lacerations of the mucosal surface of the esophagus occur with every sharp object that remains in the esophagus longer than a few hours, and only slight, temporary symptoms of pain on swallowing or a "sticking" sensation in the throat result. Severe complications such as esophageal perforation and mediastinitis are almost invariably due to the prolonged sojourn of the foreign body which results from the failure of early diagnosis. A child who complains of having a fish bone stuck in his throat will rarely have it in a position in which it is visible with a tongue depressor or even a laryngeal mirror. In the great majority of cases it is lodged in the cervical esophagus. To postpone inspection of this area by roentgenogram and esophagoscopy results in erosion and abscess formation. Blind attempts at removal result in esophageal perforation with mediastinal emphysema, pneumothorax and, in some cases, death.

Strictures of the esophagus due to foreign bodies have been encountered in several instances. In one a ten year old girl had a complete esophageal atresia due to a button which she had swallowed six years previously. No button was visualized on the most careful roentgen examinations, but after repeated esophagoscopic attempts to recannulate the esophagus, the foreign body was finally found imbedded in dense scar tissue and was eventually extracted through the mouth. Subsequent dilatations resulted in normal swallowing function.

DIAGNOSIS

To establish the diagnosis of a foreign body in the air or food passages one must carefully evaluate the history, the symptoms and the physical and roentgen studies, and then confirm or deny the diagnosis by endoscopic examination. A positive history of choking or gagging, or the statement of the patient, no matter how young, that he has swallowed something must never be ignored. Recently a two year old boy was brought to the hospital by his mother because he said he had "swallowed a red pin." He was symptom-free, but a wheeze was heard over the right chest with the stethoscope, and fluoroscopy showed a long corsage-type pin with a small head in the right bronchus, point upward, imbedded in the posterior tracheal wall. To disregard the

child's statement because of his age and lack of symptoms would have meant a delay in removal which might have resulted in a tracheoesophageal fistula. Yet no matter how strongly one relies upon a positive history to lead to a diagnosis of foreign body, a negative history is valueless or misleading. This is particularly true of infants, who may aspirate or swallow an object unobserved by an older person.

A study of the symptoms and physical findings not only aids in establishing the presence or absence of a foreign body, but also gives an accurate indication of its location. Next, and of equal importance, is the x-ray examination. This should consist in more than the interpretation of one film. It should include a complete roentgen-ray study of the patient with fluoroscopy, anteroposterior films, lateral films, comparisons of inspiration and expiration, and overexposed films.

Finally, the endoscopic procedure must be considered not only from the standpoint of therapy, i.e., removal of the foreign body, but also as a diagnostic procedure when the other examinations are inconclusive. Finding a peanut in the bronchus of a child who has a negative foreign body history, but an "unresolved pneumonia" of unknown etiology, is a common example of the diagnostic phase of the endoscopic procedure in foreign body work.

TREATMENT

The treatment of foreign bodies in the air or food passages consists in their reasonably prompt removal under conditions which will insure the maximum safety and minimum trauma to the patient. For some reason, foreign bodies are often classified as urgent emergencies leading to hasty, inadequate study and poorly prepared, improper attempts at removal. It may be stated that unless actual or potential respiratory obstruction is present, a foreign body problem is not a true emergency. True emergencies exist only when a foreign body is lodged in the larynx or trachea, or a large object is in the cervical esophagus compressing the trachea. A bean or kernel of corn in the trachea or bronchus falls into this category, since it begins to swell as it absorbs the moisture of the surrounding tissues. Similarly, a marble or a jackstone in the esophagus is usually an urgent emergency, since they cause respiratory obstruction because of compression of the trachea. Other foreign body problems may be studied without the pressure of considering an immediate endoscopy and the procedure of bronchoscopic or esophagoscopic removal scheduled when proper personnel are available, instruments are checked and techniques have been tested.

An adequate instrumentarium is essential, and failure in removal of a foreign body or the loss of a patient can never be excused or justified by the lack of proper equipment. In addition, the endoscopist must

have a thorough understanding of the fundamental principles of the mechanical problems of foreign body extraction; without such knowledge foreign body removal should not be attempted because of its many pitfalls.

Obviously only certain generalizations may be mentioned in regard to the operative procedures themselves. No patient should be operated upon with make-shift instruments. The biplane fluoroscope is indispensable in some cases (Fig. 13) and, if available, may be used when-

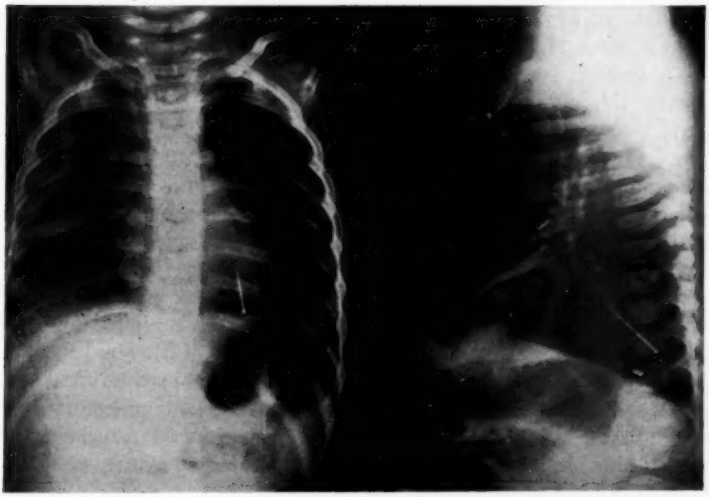

Fig. 13. Common pin in the left lower lobe bronchus necessitating biplane fluoroscopic assistance during extraction, since the pin lies in the periphery of the lung and cannot be visualized through the open tube.

ever there is any indication that it might be of assistance. In most instances no anesthesia is used for endoscopy in children, although exceptions may be made for extremely uncooperative children; however, the most serious emergencies arise during the procedures carried out under general anesthesia. These are due to pulmonary suppuration or respiratory obstruction produced by the foreign body or, if the foreign body is in the esophagus, by the pressure of the esophagoscope against the trachea. In only the rarest exception, less than 1 per cent in this series, has it been necessary to consider external surgical procedures such as thoracotomy, lobectomy, bronchotomy or mediastinotomy for the removal of a foreign body.

The management of the complications caused by foreign bodies or their extraction presents many serious problems. The management of laryngitis produced either by the foreign body or by attempts at re-

moval consists in placing the child in a "steam room" at once without waiting for the signs of obstruction. Such treatment is indicated if the laryngoscopy demonstrated evidence of laryngeal edema or if the bronchoscope met resistance in its passage through the larynx. Similarly, if the duration of the procedure was unusually long, more than ten minutes in a two year old child, for example, the "steam room" should be utilized. Since laryngeal edema is proportional to the time the tube is in the larynx as well as to the size of the tube in relation to the size of the child, the smallest-caliber tubes should always be used. The repetition of any endoscopic procedure following an unsuccessful attempt at removal should be avoided until all laryngeal symptoms which may have been present disappear completely. An exception to this rule is severe respiratory obstruction.

Antibiotics are not used after the uncomplicated removal of a foreign body. However, antibiotics in the complications of foreign bodies are of definite value and are used routinely in cases of suspected esophageal perforation or pulmonary infection; but it must be remembered that these antibiotics are no substitute for proper and adequate drainage, and in cases of bronchial obstruction unrelieved by the foreign body extraction there should be no hesitation in reaspirating a drowned lung.

Foreign bodies that reach the stomach will almost invariably pass through the gastrointestinal tract without difficulty if the child is given its regular diet without extra "roughage" and without carthartics. Under these conditions the normal bowel contents carry the object along with an almost negligible danger of obstruction or perforation; roughage and cathartics increase bowel activity, so that perforation or intussusception is more likely to occur.

The great majority of foreign bodies that have reached the stomach will pass without complications, although their position and progress should be observed radiologically by films or brief fluoroscopy every second day until they pass. If the object moves through the intestine, it is safe to be conservative and allow it to continue its advance. If it becomes stationary and remains in one position for as long as a week, surgical removal should be considered. Foreign bodies that remain loose in the stomach for a long time are generally of little concern unless they are unusually large. However, such objects as bobby pins or needles enter the stomach easily on their long axis, but in small children under two years of age have difficulty in passing through the turns of the duodenum. Bobby pins may be removed from the stomach or duodenum with magnets under fluoroscopic guidance. Frequently foreign bodies thought to be in the stomach from their position on the x-ray picture or even the fluoroscopic screen are subsequently demonstrated to be behind it when a lateral film is made or the patient is given a small quantity of barium. This is particularly true of bobby pins. Since they

may cause perforation of the duodenum, they should be removed if serial x-ray films demonstrate that they are stationary. Such removal can be accomplished by having the child swallow a small magnet on a string. After twelve to twenty-four hours the magnet attaches itself to the bobby pin, and usually the pin can be brought back into the stomach on the magnet and the magnet and pin extracted through the mouth.

The great majority of foreign bodies are removed from the air and food passages without serious complications. In the entire series of 2042 cases herein reported the total mortality was less than 0.4 per cent. Morbidity and mortality are generally the result of failure of early diagnosis. Complications developing after endoscopic attempts at removal, whether successful or not, are most often due to inadequate instrumentarium, a failure of recognition of the mechanical problem of extraction or knowledge of its solution, or too zealous and early a repeat attempt following a previously unsuccessful endoscopy.

CONCLUSIONS

Foreign bodies in the air and food passages constitute a constant hazard in all age groups. In infants and children they may be dramatically apparent as they produce severe respiratory obstruction, or they may be insidious, without a definite history, and found only on postmortem examination as the etiology of a fatal pneumonia. Certain "do's" and "dont's" may be listed as conclusions drawn from the preceding discussion.

In general,

Do

1. Believe the mother or the child who gives a history of choking on or ingesting an object, in spite of a subsequent disappearance of symptoms.
2. In case of a history suggestive of a foreign body, study the patient from the top of the nose to the bottom of the pelvis by physical examination and roentgenograms.
3. Try to obtain a duplicate of the foreign body if it is an unusual object, part of a toy, or the like, to assist in the choice of technique of extraction.

Don't

1. Don't accept a negative history if signs and symptoms suggest the presence of a foreign body. The infant may have swallowed or aspirated the object in a brief moment during which he was unobserved.

2. Don't say, "Wait and see if it will pass," if symptoms have subsided after an initial episode of coughing and choking; this may be merely the "symptomless interval" phase of a dangerous foreign body problem.

3. Don't rely on the interpretation of a single film in establishing the presence or absence of a foreign body. A child thought to have swallowed a coin may show no metallic object on the film, but a careful lateral view may reveal the tracheal compression caused by a plastic disk "tax token" in the cervical esophagus.

In Aspirated Foreign Bodies:

Do a physical examination of the chest; inspiration and expiration films are confirmatory studies.

Don't slap the child on the back. A peanut lodged in the bronchus will cause cough, wheezing and dyspnea. But if it is dislodged, though it may be expelled, it may also get caught in the larynx to cause immediate, total obstruction.

In Swallowed Foreign Bodies:

Do obtain lateral roentgenograms of the neck, chest and abdomen in addition to the anteroposterior views.

Don't use barium or cotton soaked in barium. This complicates the subsequent attempt at removal, covering the field with a white paste and necessitating the removal of the strands of cotton from the original foreign body before it can be satisfactorily manipulated for extraction. If a radiopaque substance must be used, substitute an iodized oil (Lipiodol, Iodochloral or the like) for the barium.

In Foreign Bodies in the Stomach and Intestines:

Most foreign bodies will pass spontaneously if they reach the stomach.

Do take a film (anteroposterior and lateral views) for record and repeat every second day to note progress.

Don't fluoroscope repeatedly beyond x-ray tolerance.

Do insist on a normal diet to allow the normal bowel contents to carry the foreign body onward.

Don't give apomorphine to patients with gastric foreign bodies in an effort to expel the object by vomiting. The object may lodge in the esophagus or lacerate it on return, necessitating endoscopic removal or surgical repair, whereas it will almost invariably pass by bowel if permitted to proceed without outside interference.

Do consider bobby pins and needles in the stomach and duodenum

as distinct entities. In children under two years of age they should be removed at once, perorally by magnets.

Don't give cathartics, excess roughage or "paper, cotton and string" diets in an effort to aid the passage of the object through the intestinal tract. These increase the likelihood of obstruction or perforation through mechanical block and increased peristalsis.

SUMMARY

1. From a study of 2042 consecutive cases of foreign bodies in the air and food passages, statistics are obtained showing the types of foreign bodies encountered, their location, an analysis of the age groups and various other etiologic factors. The commonest foreign bodies in children are peanuts, pennies and safety pins.

2. *The initial symptoms* of a foreign body in the air or food passages are coughing, gagging, choking and wheezing. These are followed by a *symptomless interval*, when the object becomes fixed in the bronchus or esophagus; finally, if not extracted, the *symptoms of the complications* develop (atelectasis, esophageal obstruction, infection, hemorrhage, and so on).

3. Diagnosis is dependent upon the history, physical findings, radiologic study and the endoscopic examination. A negative history is valueless and misleading. Overlooked foreign bodies are often responsible for extensive pulmonary or esophageal pathology, being discovered only on endoscopic investigation.

4. Foreign body problems are acute emergencies only if respiratory obstruction is present or pending. The treatment of foreign bodies in the air and food passages consists in endoscopic removal under visual or fluoroscopic guidance by an endoscopic team with adequate instrumentarium.

700 North Michigan Avenue
Chicago 11, Illinois

RESUSCITATION OF THE NEWBORN

PAUL D. BRUNS, M.D.

Careful prenatal care and judicious conduct of labor will do more to save babies from apnea at birth than all the resuscitating measures in the world.—N. J. Eastman, M.D., 1940.

In a recent review of patients admitted to a Special Prenatal Clinic at the Colorado General Hospital the problems surrounding prematurity and fetal anoxia overshadowed all others as a cause of respiratory embarrassment in the newborn.[39] From an analysis of the neonatal fatalities which occurred in these same patients the factors largely responsible for death involved pulmonary ventilation abnormalities. To manage this serious problem in this community "poor-risk" patients were selected for special supervision and frequently admitted to the Hospital for extra care. Results of this policy demonstrated that prematurity and anoxia could not always be prevented, but could be *controlled* by assiduous attention to the following factors: (*a*) antenatal care, (*b*) maternal disease, (*c*) obstetric complications, and (*d*) premature labor and delivery.

In a recent book[22] on artificial respiration, only six pages are devoted solely to resuscitation of the newborn. This meagerness of space suggests, among other things, a lack of reliable data on this important problem and acknowledges a certain confusion which permeates the physiopathology and treatment of respiratory distress in the neonate. Actually, since Eastman's[15] emphasis on prophylaxis, oxygen, and gentleness in resuscitation, little new has been added except for construction of complex contrivances designed to perform artificial respiration. The physiologic basis for resuscitation of the newborn has been reviewed recently in detail by Little and Tovell.[24]

From the Department of Obstetrics and Gynecology, University of Colorado Medical Center, Denver.

METHODS OF ASPIRATION

Of all the procedures advocated to resuscitate a newborn, "cleaning the air passages" enjoys the only universal popularity. One reason for this unusual agreement is the clinical observation that as a baby's air passages are being cleaned, respirations begin, thus obviating aggressive measures designed to make an infant breathe even if its lungs are congenitally absent.

Nasopharyngeal Aspiration

Perhaps the first most effective means of avoiding a respiratory problem in the newborn consists in cleaning the nose, mouth and pharynx when the infant's head first emerges over the perineum. This may be done effectively by inserting a small rubber catheter into the nares and applying suction from a mechanical device. The rubber syringe or the manual act of stroking the throat has been substituted when catheter suction is unavailable. The important factor, however, is taking time to clear the upper air passages before delivering the infant (Fig. 14).

Tracheobronchial Aspiration

When the infant has been delivered, the nasopharynx further cleared, but respirations do not begin, a catheter is passed into the trachea, preferably by direct laryngoscopy. The virtues of this procedure have been well documented and its dangers considerably overemphasized. Careful examination of the larynx and trachea following intubation in 155 neonatal fatalities in this department failed to show the epithelial damage often quoted in the literature. However, the danger of producing additional shock in premature infants under 4 pounds by the immediate or delayed use of tracheobronchoscopy is well worth noting.[34]

Gastrointestinal Aspiration

This innovation has been highly recommended for babies born by cesarean section or by difficult vaginal delivery. Since respiratory movements and deglutition occur during normal intrauterine life and more frequently when the fetus becomes anoxic, the possibility of preventing pulmonary complications by clearing the stomach has merit. At cesarean section an infant's stomach usually contains 14 to 20 cc. of fluid. If this material is removed at the time of delivery and periodically thereafter, the probability of regurgitation and aspiration of stomach contents should be greatly decreased. If the aspiration of stomach contents plays an important role in the pathogenesis of pulmonary complications

A

B

Fig. 14. Nasopharyngeal aspiration *during* delivery. A, Rubber catheter—mechanical suction. B, Rubber bulb—manual suction.

in the newborn as many[1, 20, 25, 35] suggest, this may constitute an important prophylactic procedure (Fig. 15).

Gravity Aspiration

Most authorities agree that a "head-down" position will aid in the drainage of amniotic fluid from the lungs.[21] Disagreement exists on the degree of inclination that is most effective and safe. Somewhere between 15 and 30 degrees Trendelenburg offers the advantages of gravitation without incurring the disadvantage of abetting intracranial

hemorrhage. Certainly holding the infant up by the heels and gyrating it carries with it a risk equal to the hazard of aspirating mucus and amniotic fluid.

A

B

Fig. 15. Gastrointestinal aspiration *after* delivery. *A*, Aspiration via the mouth—heated bassinet. *B*, Aspiration via the nasopharynx—15 degrees Trendelenburg.

Umbilical Cord Care

After expulsion of the infant careful consideration should be given to the fetal blood remaining in the placenta and cord. If factors of isoimmunization or transplacental narcosis are imminent, immediate clamping of the umbilical cord is obviously indicated. In the majority of instances of normal or abnormal labor certain benefits are available to the newborn if the placental blood is allowed to drain back to the infant. Studies on this aspect of fetal physiology have shown that the combination of vasoconstriction, uterine contractility and gravity can

furnish an autotransfusion of 37 to 187 ml. if the umbilical cord is not suddenly severed. Therefore, to offer a newborn an immediate increase in oxygen-carrying capacity, an increased blood volume and blood pressure and the later benefit of an ample iron reserve seems well worthwhile. To obtain this added advantage for a baby the umbilical cord is allowed to cease pulsating before clamping. When this principle is used, it usually takes twenty minutes before pulsations stop. This indicates that blood is no longer flowing from the infant to the placenta. Since it is seldom possible to wait so long and because three fourths of the trapped blood will be transported to the fetus within three minutes after delivery, *delayed clamping of the cord* becomes a more feasible procedure. To obtain the maximum amount of blood for the fetus in the shortest possible time, the combination of holding the *infant below the level of the mother* and gently *stripping the umbilical cord* eight to ten times will provide a rather complete transfusion quickly and atraumatically,[3, 11, 12, 17, 27, 28, 42]

METHODS OF RESUSCITATION

The various types of resuscitation may be divided broadly into single- and double-phase systems. Although this division applies more directly to artificial resuscitation of the adult, the principles, for the most part, apply to the newborn. When forcible expiration or inspiration is used, the terms "single phase," "monophase," "push" or "pull" are applicable. If both expiration and inspiration are used together as a push-pull mechanism, the system is called double-phase or diphasic respiration. Most methods of artificial respiration are designed to produce a flow of gases in and out of the lungs by increasing or decreasing the size of the thoracic cavity. But many of these methods of resuscitation are not applicable to the newborn because they presuppose that expanded lung tissue is available and capable of function. The primary effort in the apneic newborn consists in initially expanding a sufficient number of alveoli to provide an adequate exchange of gases. After the alveoli have been opened, the respiratory epithelium must be mature enough to function.

Manual Resuscitation

Most maneuvers designed to establish pulmonary ventilation in the apneic newborn involve attempts to change the size of the thoracic cage. Probably the earliest but less physiologic of methods, and one still used, is compression of the chest and abdomen, or flexion of the body. Techniques which attempt to accomplish the same by displacement of the abdominal viscera include teetering or rocking the newborn.[18, 31]

With the exception of the gentler methods of resuscitation, most of the fantastic maneuvers described in the literature are not generally used because they increase existing intracranial hemorrhage, produce rupture of the liver, and contribute to circulatory shock. From the findings in the autopsy room it would seem advantageous to the infant if gentleness in manual resuscitation was used rather than a favorite method of artificial respiration.

Mechanical Respiration

Mouth-to-mouth artificial respiration probably represents the oldest known method of insufflation. It has been modernized by the use of catheters, pressure gauges, filters and prophylactic antibiotics, and it is still recommended as an acceptable emergency procedure outside the hospital. The pressures suggested are those comparable to "blowing small smoke rings"[30] or 20 cm. of water pressure.

Intermittent Positive Pressure. This method is used for resuscitating a newborn at the Colorado General Hospital. The apparatus, a Kreiselman infant resuscitator,[23] can deliver controlled pressures by face mask at rhythms determined by the operator, but cycled to the infant (Fig. 16). The machine is also equipped with a heated bassinet, continuous flow mask and an electric aspirator. This method of resuscitation has been championed for many years, but has been challenged on the theoretical grounds that it impedes circulation and ruptures alveoli if misused.

If positive pressures are used to initially expand alveoli, they should approach 20 cm. of water pressure. The range of safety is narrow; 10 to 20 cm. of water pressure are usually necessary for initial expansion of alveoli, while 25 cm. of water pressure or over may cause alveolar rupture. However, as noted by R. Day[10] and Wilson,[43] it is not only the pressure that is important, but also the time of exposure and the amount of expandable lung tissue available. In a study of 390 fetal and neonatal deaths by McFarland at the University of Colorado Hospitals[29] one infant fatality was due to alveolar rupture following the inadvertent use of high pressure oxygen delivered through an endotracheal catheter. This misuse has frequently been misjudged as a serious disadvantage of positive pressure oxygen.

The administration of 100 per cent oxygen by an intratracheal catheter with intermittent positive pressure is also an acceptable form of therapy for the apneic infant. Flagg[19] in this country and Blaikley[6] in England have recommended this method of administering oxygen. If a catheter is placed in the trachea atraumatically and controlled pressures are used, absorption of oxygen at some level in the respiratory

tract is usually sufficient to oxygenate the infant's blood. Inexperience and excessive pressures tend to be overemphasized. The principal danger in administering oxygen by this method appears to be that of producing shock in very small premature infants.

Fig. 16. Kreiselman infant resuscitation. A, Intermittent positive pressure—face mask. B, Continuous flow oxygen—face mask.

Intermittent Negative Pressure. This may be accomplished in an apparatus such as the Drinker-Infant respirator. The infant's body is enclosed in the chamber with the head outside. Intermittent negative pressures are applied around the body and automatically cycled. The machine usually cannot be regulated to the infant's respiratory pattern and does not enhance cardiac filling.

Alternating Positive-Negative Pressure. Actually, there is little difference between the various methods of intermittent pressures except as to whether the negative phase goes lower than 760 mm. of mercury. Commonly included in this category are the "suck and blow" machines. Recently a "servo-patient-cycled" apparatus has been recommended to augment respirations.[13] By electronic devices the infant's respiratory movements control the machine's activity. In eight cases of atelectasis reported by these workers, four were possibly aided by this method of resuscitation.

When an infant is placed in a closed chamber or sealed airlock and alternating pressures are used, oxygen is "packed" into the alveolus to accomplish artificial respiration. No change in the size of the thoracic cavity occurs. Whatever virtues or limitations these mechanical devices have, they certainly "dispose of handling the infant by the M.D. or R.N."[7]

Electrosurgical Resuscitation. Electrophrenic artificial respiration is accomplished by intermittently stimulating the phrenic nerves. A recent critical and excellent evaluation of this form of resuscitation has been presented by L. Day.[9] Although physiologically sound and known for a hundred years, electrophrenic respiration is still considered to be in the developmental stage.

Berglund[5] has reported favorably on three infants given positive pressure insufflation during open thoracotomy. Love[26] applies a towel clip to the lower sternum, and attaches it by rubber bands to the top of an incubator and leaves it in place for one to three days as a method of augmenting respirations.

Gastrointestinal Oxygen. In 1935 Ylppo[44] suggested the use of oxygen administered into the stomach of apneic prematures. He demonstrated that the gastric mucosa was capable of absorbing oxygen. In 1950 Akerren[2] reported on the intestinal administration of oxygen. He placed two catheters in the stomach and attached one to oxygen given at the rate of 3 to 4 liters per minute. He reported favorably on six cases treated in this fashion. Waller in 1953[41] and Toaff a year later[40] each reported on a series of approximately forty-five cases. Toaff stated that the method was simple and nontraumatic to lungs, gave quick results, and was a valuable method of oxygenating the handicapped newborn. This method of gastrointestinal administration of oxygen seemed reasonable to Toaff because the mucosa is a highly vascular bed, diffusion was favored by the low oxygen in the infant's blood, and absorption was encouraged by acidosis and the affinity of fetal hemoglobin for oxygen. He also used two catheters, but gave oxygen at 2 to 3 liters per minute. He cautioned that even though gastrointestinal oxygen is used as the method of resuscitation, clearing of the air passages still remained an important factor.

DISCUSSION

It is difficult to assess the worth of any particular method or mechanical apparatus in resuscitating an apneic newborn. The small number of cases needing resuscitation, the difficulty in obtaining comparable control series, the differentiation between anoxia, intracranial hemorrhage, narcosis and the element of the "voice of experience" makes any classification of the cause of apnea and the adequacy of treatment well nigh impossible. However, this apparent impasse should not be a deterrent to the continued study of untried methods and devices for artificial resuscitation.

Causes of Respiratory Difficulty in the Newborn

From the obstetrician's point of view the most important clinical aspect of respiration difficulties in the newborn is the prevention of premature birth. Although this cannot be done with certainty, it may be averted if women with abnormalities are treated medically, surgically and psychologically prior to or early in pregnancy. It may also be improved by careful diagnosis and treatment of complications of pregnancy which predispose to prematurity, such as hemorrhage, toxemia and infection. The gentle management of premature labor and delivery and resuscitation of the newborn can further reduce the number of respiratory problems in the perinatal period.

Analgesia and Anesthesia. It is difficult to prove that respiratory depressing agents or conduction anesthetics which produce hypotension in the mother are absolute causes of apnea and death in the newborn. Nevertheless, heavy maternal analgesia and anesthesia may be contributory causes of neonatal death. When analgesia and anesthesia are thought to be involved in a fetal death, careful study should be given to the amount of drug used, route of administration, time relationship to clamping of the cord, change in fetal heart rate, amniotic fluid or maternal blood pressure, and the physician's judgment and skill in administering the anesthetic.

In the five year period from July 1, 1948, through June 30, 1953, at the Colorado General Hospital there were 585 premature infants delivered alive weighing between 400 and 2500 gm. Of this number eighty-nine died in the early neonatal period, giving a mortality rate of 15 per cent. Autopsies were done on 96 per cent of these infants. In six infants analgesia and anesthesia were implicated in the cause of death. Although analgesia and anesthesia could not be incriminated as the primary cause of death, medullary depression was considered a contributory cause.

No statistical significance was associated with this analysis; nevertheless certain biologic impressions evolved from the study of each case.

These can be arbitrarily summarized as follows: (*a*) Untreated hypotension may lead to fetal anoxia. (*b*) Intravenous use of maximum doses of narcotics one hour prior to delivery offers the optimum chance of transplacental narcosis. (*c*) Uterine inertia may be produced by conduction and systemic analgesia given too early in labor. (*d*) Heavy premedication for cesarean section may be responsible for a difficult resuscitation. (*e*) Systemic anesthesia superimposed on a narcotic or barbiturate analgesia may cause marked respiratory depression in the infant. With or without statistical proof, systemic analgesics and anesthetics should be used sparingly, given at the right time, and eliminated when possible; when they are used in excessive amounts, the mother and infant should be surrounded with all the safeguards necessary to insure an atraumatic resuscitation.

Difficult Deliveries. Taylor has pointed out the desirability of eliminating difficult midforceps deliveries as a means of further reducing perinatal complications. In the last 10,000 deliveries at the Colorado General Hospital this operation was elected thirty-one times and resulted in a 26 per cent total fetal mortality plus a 22 per cent incidence of fetal morbidity.[38] Needless to say, resuscitation problems surrounding traumatic delivery in this Clinic have been markedly reduced by the elimination of difficult forceps deliveries. There has been no concomitant increase in cesarean section rate, and no infants delivered by cesarean section have succumbed to "drowning in aspirated amniotic fluid" since this change in obstetric policy.

Analeptics. The use of drugs to stimulate an already well stimulated medulla is unphysiologic and occasionally can be hazardous.[14] In recommended doses or those usually elected for emergencies, analeptics may precipitate convulsions, hypertension and tachycardia and accentuate the degree of existing anoxia, respiratory depression and secondary atelectasis.

When medullary depression in an infant results from heavy analgesics combined with systemic anesthesia at delivery, careful observation will reveal a shallow, almost imperceptible type of respiratory movement. Although this volume of air exchange may not be great enough for the attendant's peace of mind, it is usually adequate for oxygenation of the infant and does not warrant aggressive resuscitative measures. However, the use of a specific antagonist to morphine or derivatives may be desirable and is acceptable. Such a drug, Nalorphine,[8, 16, 33] may be given prophylactically to the mother in the amount of 10 mg. ten minutes prior to delivery. It may also be administered in doses of 0.1 mg. via the umbilical vein at delivery. Since Nalorphine is antagonistic only to morphine or its derivatives, no "stimulating" effect can be expected if it is given to a normal infant or to counteract barbiturate, cyclopro-

pane and ether anesthesia. Indeed, it may behave synergistically with ether to further depress the respiratory center.

Chest Roentenograms. It is usually not desirable to obtain a roentgenogram of an infant's chest prior to the first breath of life, but it may be of value to take one shortly after resuscitation. A properly taken chest roentgenogram may be helpful in assessing the degree of pulmonary expansion following resuscitation. Likewise, pulmonary complications which occasionally go unnoticed, such as pneumothorax and congenital anomalies, may be found. In respiratory problems revolving about the so-called hyaline-like membrane disease, the diagnosis and prognosis of this entity in the living infant may be made possible by roentgenographic research. In any event the more frequent use of chest roentgenograms will account for more accurate diagnosis of pulmonary pathology and better treatment of handicapped newborns and will possibly aid in the diagnosis of some of the more obscure respiratory diseases.

Oxygen Toxicity. Oxygen poisoning is not a new concept.[4,37] Priestley entertained an idea of its noxious effects soon after he had isolated it in 1775. Paul Bert, 100 years later, stated that oxygen played a dual role in sustaining life at low pressures and killing at higher pressures. Acute oxygen poisoning occurs at partial pressures above 3.5 atmospheres and may cause sudden death by convulsions and coma without demonstrable pathologic changes. Subacute oxygen poisoning requires longer exposures at 0.7 to 1.0 atmosphere. This type causes characteristic pulmonary changes which result in anoxia and death within a few days. It is this variety of oxygen poisoning which may theoretically affect a newborn infant's lung. The gross pulmonary changes of subacute oxygen poisoning in animals are mottled, liver-like lungs which sink in formalin or water. The microscopic panorama of this lesion includes edema, congestion, hemorrhage, infection and hyaline-like membrane formation. From a summary of the literature on oxygen toxicity one may conclude that oxygen can behave as a poison, depending primarily upon factors of partial pressure and duration of exposure.

After an infant has been resuscitated by 100 per cent oxygen it would seem judicious to place the baby in an environment of oxygen less than 70 per cent for short periods to avoid any possible toxic effects of high concentrations of oxygen.[36]

Hypothermia. In the literature on resuscitation of the newborn most authorities agree that warmth is an important factor in a handicapped infant's survival. However, recent reports[29] based upon hypothermic experiments in guinea pigs suggest that chilling may prove effective in the treatment of asphyxia of the newborn. This approach is, of course, as yet in the experimental stage.

SUMMARY OF MANAGEMENT OF RESPIRATORY PROBLEMS IN THE NEONATE

Prevention of Prematurity

Preconceptional Care. This should include correction of organic and functional disease, supplementary high vitamin and protein diet, and special studies for patients with poor obstetric histories.

Prenatal Care. This calls for early complete examination, detailed antenatal education and frequent visits, low sodium and high vitamin-protein-mineral diet, and adequate physical and mental rest.

Control of Prematurity

Correction of Maternal Disease. Disease in the prospective mother requires nutritional supplements or blood transfusions for anemia, detection and adequate treatment of infections, insulin and delivery three to four weeks early in diabetics, and medical consultation and added rest for heart disease.

Management of Obstetric Conditions. Bed rest is indicated after the thirtieth week for multiple pregnancies. A low sodium diet and rest or hospitalization are called for in pre-eclampsia. Placenta previa should have expectant treatment. There should be pediatric and obstetric consultation on Rh problems.

Treatment of Premature Rupture of the Membranes

Bed rest is indicated, preferably in the hospital. Antibiotics or sulfonamides and vitamin K should be administered. The number of vaginal or rectal examinations should be kept to a minimum. Labor should not be induced.

Management of Premature Labor and Delivery

Oxygen and intravenous glucose solution are administered to the mother for fetal distress. Psychoanalgesia and local anesthesia should be given to aid in the delivery, which should be spontaneous with a generous episiotomy. Dührssen's incisions should be made in complicated breech deliveries. No narcotics, barbiturates or oxytocics should be given.

Resuscitation of the Handicapped Newborn

The nasopharynx should be aspirated *during* delivery. It is well to delay clamping of the umbilical cord. After delivery the infant should

be placed in a 15 to 30 degree Trendelenburg position and should have tracheal and gastric suction. Intermittent positive pressure resuscitation should be instituted within two minutes (100 per cent oxygen at 20 cm. of water pressure for 0.2 second's duration). Ten minutes before delivery Nalorphine, 10 mg., should be injected in a maternal vein; after delivery 0.1 mg. should be injected in the umbilical vein. If the infant is delivered outside the hospital, rocking methods or mouth-to-mouth resuscitation may be tried. After resuscitation has been completed the infant should be maintained in an atmosphere of 50 per cent oxygen and 100 per cent humidity.

REFERENCES

1. Ahvenainen, E. K.: A Symposium on Anoxia of the Newborn Infant. Springfield, Ill., Charles C Thomas, 1953, p. 113.
2. Akerren, Y., and Fürstenberg, N.: Gastro-intestinal Administration of Oxygen in Treatment of Asphyxia in Newborn. J. Obst. & Gynaec. Brit. Emp., *57*:705, 1950.
3. Ballentine, G. N.: Delayed Ligation of Umbilical Cord. Pennsylvania M. J., *50*: 726, 1947.
4. Bean, J. W.: Effects of Oxygen at Increased Pressure. Physiol. Rev., 25:1, 1945.
5. Berglund, E., and Eder, W. P.: Surgical Approach to Atelectasis of Newborn Infant; Preliminary Report. Surgery, 29:127, 1951.
6. Blaikley, J. B., and Gibberd, G. F.: Asphyxia Neonatorum; Its Treatment by Tracheal Intubation. Lancet, *1*:736, 1935.
7. Bloxsom, A.: Resuscitation of Newborn Infant; Use of Positive Pressure Oxygen-Air Lock. J. Pediat., 37:311, 1950.
8. Chalmers, J. A., and Thornberry, C. J.: N-Allylnormorphine (Lethidrone) in the Treatment of Neonatal Asphyxia. J. Obst. & Gynaec. Brit. Emp., *61*: 244, 1954.
9. Day, R. L.: Electrophrenic Artificial Respiration in the Newborn. Unpublished data, 1954.
10. Day, R. L., Goodfellow, A. M., Apgar, V., and Beck, G. J.: Pressure-Time Relations in Safe Correction of Atelectasis in Animal Lungs. Pediatrics, *10*:593, 1953.
11. DeMarsh, Q. B., Alt, H. L., and Windle, W. F.: Effect of Depriving Infant of Its Placental Blood on Blood Picture during First Week. J.A.M.A., *116*:2568, 1941.
12. DeMarsh, Q. B., Windle, W. F., and Alt, H. L.: Blood Volume of Newborn Infant in Relation to Early and Late Clamping of Umbilical Cord. Am. J. Dis. Child., *63*:1123, 1942.
13. Donald, L., and Lord, J.: Augmented Respiration. Studies in Atelectasis Neonatorium. Lancet, *1*:9, 1953.
14. Draper, W. B., and Whitehead, R. W.: Chances of Resuscitation after Overdose of Ether, Divinyl Ether and Chloroform. Lancet, *1*:422, 1942.
15. Eastman, N. J.: Apnea Neonatorum. Am. J. Obst. & Gynec., *40*:647, 1940.
16. Eckenhoff, J. E., Hoffman, G. L., and Funderburg, L. W.: N-Allylnormorphine: An Antagonist to Neonatal Narcosis Produced by Sedation of the Parturient. Am. J. Obst. & Gynec., *65*:1269, 1954.
17. Editorial comment. Obst. & Gynec. Survey, 2:618, 1947.
18. Eve, F. C., and Forsyth, N. C.: Asphyxia of Newborn Treated by Rocking. Brit. M. J., 2:544, 1948.
19. Flagg, P. G.: Treatment of Asphyxia in the Newborn: Preliminary Report of the Practical Application of Modern Scientific Methods. J.A.M.A., *91*:788, 1928.

20. Gellis, S. S., White, P., and Pfeffer, W.: Gastric Suction: A Proposed Additional Technique for Prevention of Asphyxia in Infants Delivered by Cesarean Section. New Eng. J. Med., 240:533, 1949.
21. Gibberd, G. F.: A Symposium on Anoxia of the New-Born Infant. Springfield, Ill., Charles C Thomas, 1953, p. 26.
22. Karpovich, P. V.: Adventures in Artificial Respiration. New York, Association Press, 1953.
23. Kreiselman, J.: Treatment of Asphyxia. South M. J., 38:598, 1945.
24. Little, D. M., Jr., and Tovell, R. M.: Collective Review: Physiological Basis for Resuscitation of Newborn. Surg., Gynec. & Obst., 86:417, 1948.
25. Little, D. M., Jr., D'Andrea, F. H., and Mastrangelo, A., Jr.: Gastric Aspiration as Technique for Prevention of Asphyxia in Newborn Infant. Surg., Gynec. & Obst., 93:363, 1951.
26. Love, W. G., and Tillery, B.: New Treatment for Atelectasis of the Newborn. Am. J. Dis. Child., 86:423, 1953.
27. McCausland, A. M., Holmes, F., and Schumann, W. R.: Management of Cord and Placental Blood and Its Effect upon Newborn. California Med., 71:190, 1949.
28. McCausland, A. M., Holmes, F., and Schumann, W. R.: Management of Cord and Placental Blood and Its Effect upon Newborn. West. J. Surg., 58:591, 1950.
29. McFarland, P. J.: Fetal and Neonatal Mortality. Five-Year Study From University of Colorado Hospitals, 1947–1951. Thesis submitted to the Faculty of the Graduate School, University of Colorado, 1952.
30. Mathieu, A., and Homan, A.: Resuscitation of Asphyxiated Newborn. J.A.M.A., 92:1917, 1929.
31. Millen, R. S., and Davies, J.: See-Saw Resuscitator for Treatment of Asphyxia in Newborn. Am. J. Obst. & Gynec., 52:508, 1946.
32. Miller, J., and Miller, F.: Science News Letter, 65:31, 1954.
33. New and Nonofficial Remedies. Philadelphia, J. B. Lippincott Company, 1953, p. 23.
34. O'Brien, D., and Roberts, H.: Endotracheal Insufflation with Oxygen in the Treatment of Asphyxia Neonatorum. Brit. M. J., 2:963, 1952.
35. Rhaney, K., and MacGregor, A. R.: Pneumonia in Newborn. Resuscitation for Inhalation of Gastric Contents. Arch. Dis. Childhood, 23:116, 1948.
36. Shields, L. V.: A Study of Hyaline-Like Membranes in Newborn Infants; Review of Oxygen Poisoning; Experimental Production of Hyaline-Like Membranes in Laboratory Animals. Thesis submitted to the Faculty of the Graduate School, University of Colorado, 1954.
37. Stadie, W. C., Riggs, B. C., and Haugaard, N.: Oxygen Poisoning. Am. J. M. Sc., 207:84, 1944.
38. Taylor, E. S.: Can Mid-Forceps Operations be Eliminated? Obst. & Gynec., 2: 302, 1953.
39. Taylor, E. S.: Report on Colorado Premature Infant Care Program, June 1, 1954.
40. Toaff, R., and Eckerling, B.: Gastro-intestinal Administration of Oxygen in Asphyxia of the Newborn. Obst. & Gynec., 3:366, 1954.
41. Waller, H. K., and Morris, D.: Resuscitation of the Newborn with Intragastric Oxygen (Akerren's Method). Lancet, 165:951, 1953.
42. Windle, W. F.: Aspects of Foetal Physiology. New York, Paul B. Hoeber, Inc., 1950, pp. 152–168.
43. Wilson, J. L.: Factors Involved in the Production of Alveolar Rupture with Mechanical Aids to Respiration. Pediatrics, 13:146, 1954.
44. Ylppo, A.: Ueber die Behandlung der Atemstörungen bei Frühgeburten durch direkte Zufuhr von Sauerstoff in den Magen. Acta paediat., 17:122, 1935.

4200 East 9th Avenue
Denver 20, Colorado

CARDIAC EMERGENCIES

ALEXANDER S. NADAS, M.D.

The commonest cardiac emergencies in adults are infrequently, if ever, encountered in children: myocardial infarction, cardiac asthma, vascular accidents are phenomena almost unknown to the pediatrician. Cardiac emergencies in children consist principally in attacks of paroxysmal tachycardia, "anoxic spells" of cyanotic congenital heart disease and acute congestive failure. Less common but equally serious emergencies are pericardial tamponade and Stokes-Adams attacks.

PAROXYSMAL TACHYCARDIA

Paroxysmal tachycardia is the sudden appearance of rapid heart action originating from a focus other than the sino-atrial node. After a period lasting from minutes to several days, or longer, the attack ceases just as instantaneously as it began.

Etiology

The etiology of paroxysmal tachycardia can rarely be determined with accuracy. In about half of the cases, infection, congenital heart disease and drugs appear as possible contributing factors. The remaining half of the patients show no such correlations; they are infants four months of age or younger, usually males without any concomitant disease.

Symptoms and Signs

Although paroxysmal, rapid heart action is occasionally discovered during a routine physical examination in an otherwise well child, the

From the Sharon Cardio-Vascular Unit of the Children's Medical Center and the Department of Pediatrics, Harvard Medical School, Boston.

majority of the infants are severely ill. The presenting symptoms are anorexia, irritability alternating with sleepiness, rapid respirations, cough and poor color. Careful questioning will elicit complaints about oliguria, excessive perspiration, vomiting and unexplained weight gain. On physical examination the patient often appears desperately sick; the color is ashen gray or cyanotic, respirations are rapid and labored, and the pulse is rapid and often uncountable. The temperature is normal or only slightly elevated. The skin is cold and clammy. The heart appears enlarged. Systolic murmurs of rather low intensity are present in about one third of the cases. Facial edema and an enlarged liver are often encountered.

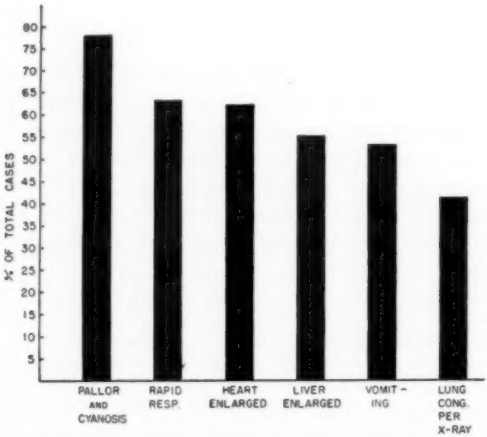

Fig. 17. Signs and symptoms in paroxysmal tachycardia. (Adapted from Nadas, A. S., et al in Pediatrics, Vol. 9, published by Charles C Thomas, Springfield, Ill.)

The *laboratory findings* are usually noncontributory except for moderate polymorphonuclear leukocytosis in about one third of the cases.

The *radiologic picture* uniformly shows cardiac enlargement and pulmonary vascular congestion of varying degrees. The cardiomegaly involves both ventricles. Not infrequently the impression of an enlarged left atrium can be discovered on the barium-filled esophagus.

The *electrocardiogram* is the most important tool in the diagnosis of paroxysmal tachycardia. The three standard limb leads usually suffice to make the diagnosis: they will reveal uniformly (1) a regular rate of 160 to 330, and (2) absence of normal P waves and P-R intervals.

The electrocardiogram is the only certain means by which the paroxysmal tachycardias—diagnosed on the basis of the two foregoing criteria—can be divided into supraventricular and ventricular types.

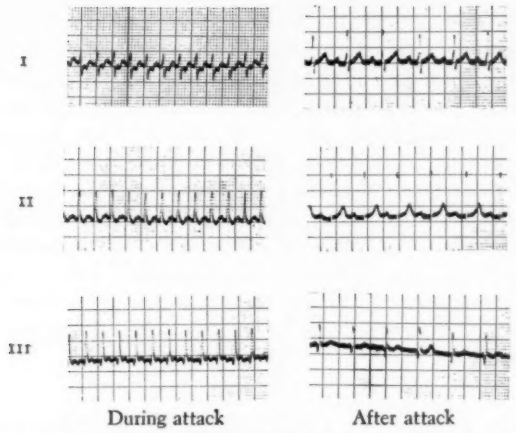

Fig. 18. Electrocardiogram of paroxysmal atrial tachycardia during and after an attack. Note absence of normal P waves and presence of normal-looking QRS complexes during the attack.

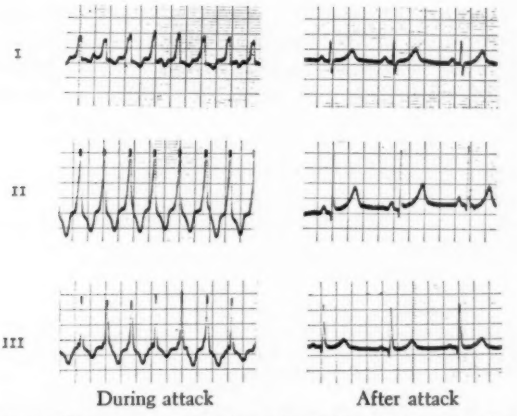

Fig. 19. Electrocardiogram of ventricular tachycardia during and after an attack. Note absence of P waves and abnormal-looking QRS complexes during the attack.

The supraventricular tachycardias are characterized by a strict regularity of the rate and by the normal-looking, narrow QRS complexes, identical with the ones seen in the same patient between attacks (Fig. 18). Ventricular tachycardias, by contrast, are not quite as regular, and the QRS complexes are wide, bizarre-looking and strikingly different from the complexes observed at normal rates (Fig. 19).

Diagnosis

The diagnosis of paroxysmal tachycardia is usually not difficult if the physician bears the possibility in mind when encountering a sick infant, usually a male less than four months old, with evidences of congestive failure and a regular heart rate of 160 or more. Sinus tachycardia with infection (most commonly pneumonia) or congestive failure is the most common problem in differential diagnosis. If an electrocardiograph is available, the discovery of normal-shaped P waves and normal P-R interval decides the question easily. Without the aid of a cardiograph, sinus tachycardia may be recognized by the relatively slower rate and the absence of clocklike regularity. The presence of infection manifests itself by high temperature and by the signs and symptoms of the infectious focus.

Management

Management of the acute attack (Tables 11 and 12) is rewarding. The individual paroxysm, if recognized and promptly treated, can successfully be terminated in the vast majority of instances. If possible, all patients with an initial attack of paroxysmal tachycardia should be cared for where an electrocardiograph is readily available, preferably in a hospital. This is necessary in order to determine the type of tachycardia one is dealing with and to assess the effect of various therapeutic procedures.

TABLE 11. *Effect of Treatment in Paroxysmal Tachycardia*

	SUPRAVENTRICULAR	VENTRICULAR
Reflex vagus stimulation*	+	0
Digitalis	+	0
Prostigmin	+	0
Quinidine	0	+
Pronestyl	0	+

* Carotid sinus pressure, eyeball pressure, induced vomiting.

After the diagnosis has been established, all patients should have a trial of carotid sinus pressure and eyeball pressure. Both these maneuvers should be performed only on one side at a time, for thirty to sixty seconds. If this is not successful, older children can usually be induced to vomit by means of syrup of ipecac, 1 or 2 teaspoonfuls at fifteen minute intervals. If these measures do not terminate the attack or if the child is too small or too sick to be subjected to them, specific drug therapy is indicated.

In supraventricular tachycardia, digitalis is the drug of choice. We have

TABLE 12. *Dosage of Drugs Used in Pediatric Cardiac Emergencies*

DRUG	ROUTE OF ADMIN.	DOSE		TOXICITY	INDICATIONS
		Initial	Maintenance		
Digitoxin ("Digitaline Nativelle")	P.O. or I.M.	<2 yrs.: 0.02–0.03 mg./lb. >2 yrs.: 0.01–0.02 mg./lb.	1/10 initial dose daily	Nausea, vomiting, arrhythmias, prolonged P-R	Congestive failure, paroxysmal atrial tachycardia
Lanatoside C ("Cedilanid")	I.M. or I.V.	As above	1/3–1/2 initial dose daily	Similar to digitoxin	Same
Quinidine	P.O. or I.M.	25–50 mg. test dose	100–400 mg. q̄ 4 hrs.	Nausea, vomiting, tinnitus, widened EKG complexes, ventricular arrhythmias	Ventricular arrhythmias
Procaine amide ("Pronestyl")	P.O. or I.V.	7 mg./lb. 50–300 mg.	50–300 mg. q̄ 6 hrs.	Hypotension, ventricular arrhythmias	Ventricular arrhythmias
Neostigmine ("Prostigmin")	S.C.	0.05–0.5 mg.	.....	Hyperactivity of gastrointestinal tract, muscular twitching, and hypotension	Paroxysmal atrial tachycardia
Epinephrine	I.M. intracardiac	0.05–0.5 mg.	.....	Tachycardia, hypertension, restlessness	Cardiac arrest, hypotension
Ephedrine	P.O. or I.M.	1.7 mg./10 lbs.	q̄ 6 hrs.	Similar to epinephrine	Slow idioventricular rhythm
Morphine	S.C.	1 mg./10 lbs.	q̄ 4 hrs.	CNS depression, respiratory failure, vomiting	Anoxic spells, excitement with arrhythmias, pulmonary edema
("Mercuhydrin")	I.M.	0.1–1 cc.	Same	Cramps, "low sodium syndrome," acidosis, dehydration	Congestive failure
("Apresoline")	P.O. I.M.	10–50 mg. 0.1 mg./lb.	4 × daily q̄ 4 hrs.	Hypotension, headaches	Hypertension
Protoveratrine	P.O. or I.V.	0.5–1.0 mg. 0.5–1.0 microg./lb.	Repeat 4 × daily Repeat every 30 minutes	Hypotension, nausea and vomiting	Hypertension
Magnesium sulfate	I.M. or I.V.	25% sol. 0.1 cc./lb. 3% sol. 75–100 mg./lb. over a 1° period	Repeat every 4–6 hours Repeat as necessary	Paralysis, respiratory failure, bradycardia, hypotension	Hypertension

been using digitoxin (digitaline Nativelle) by mouth or intramuscularly, and lanatoside C (Cedilanid) intravenously. Oral or intramuscular administration is recommended if the patient is not desperately ill, whereas, in a real emergency, the intravenous route is preferred. The digitalizing dose for both digitoxin and lanatoside C is between 0.02 and 0.03 mg. per pound for infants up to two years of age and 0.01 to 0.02 mg. per pound for children two years or older. This should be administered in three divided doses at six-hour intervals in the case of digitoxin and four-hour intervals in the case of lanatoside C. This dosage schedule was successful in the treatment of all but one of the supraventricular tachycardias we have encountered at the Children's Hospital in the past twenty-five years.[1] The one patient who did not respond favorably to this regimen was successfully treated by Prostigmin subcutaneously in doses of 0.05 to 0.5 mg. Our Clinic had a rather limited but unfavorable experience with Mecholyl; hence we do not recommend it.

The drugs of choice in the treatment of ventricular tachycardia are quinidine or procaine amide (Pronestyl) (Table 12). We have had more experience with quinidine. After an initial test dose of 25 to 50 mg., 100 mg. orally every three hours for three doses are recommended. If this is not successful in terminating the tachycardia, 150 mg. every three hours for three doses are given. In this way one increases the dose by 50 mg. either until the paroxysm ceases or until signs of quinidine toxicity appear. Nausea, vomiting and tinnitus are the clinical evidences of quinidine toxicity. Electrocardiographic evidences of such are the prolongation of the QRS complex of more than 50 per cent and appearance of multifocal premature beats. Pronestyl in the treatment of ventricular tachycardia should be administered intravenously and under cautious electrocardiographic control. The dosage in pediatrics has not been worked out in detail. We have been using an initial intravenous dose of 50 mg. followed by an increase of 25 mg. every fifteen minuites until the desired effect is accomplished. Seldom has it been necessary to increase the individual dose above 300 mg. Pronestyl toxicity manifests itself in hypotension and the appearance of multifocal premature beats. Appearance of these signs warrants discontinuing the drug.

As a supporting measure in the treatment of paroxysmal tachycardia, the use of oxygen is recommended. Antibiotics should be administered to combat or prevent infection. Morphine sulfate in doses of 1 mg. per 10 pounds should be given to patients who are restless and irritable. The diet during the attack should consist entirely of liquids. If the patient vomits, milk should be omitted and clear liquid substituted.

Prognosis

The prognosis of paroxysmal tachycardia is usually good in terms of the outcome of the individual attack; in our experience all the fatalities but one were due to faulty management or related disease (i.e., congenital heart disease). Recurrences are common, however. Two thirds of the patients had recurrences. If the initial attack occurred within the first three months of life, there was only a 20 per cent probability of recurrences beyond a year after the first attack. By contrast, 83 per cent of the children whose initial paroxysm occurred beyond four months of age continued to have recurrences several years later (Fig. 20).

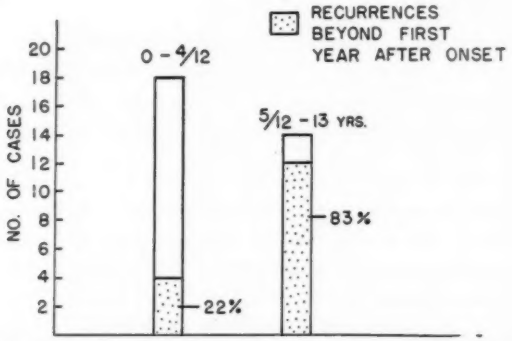

Fig. 20. Recurrences of tachycardia in relation to age at onset in 32 cases followed up for more than one year. (Nadas, A. S., et al in Pediatrics, Vol. 9, published by Charles C Thomas, Springfield, Ill.)

Prevention of recurrences is usually possible, either with digitalis or quinidine. Our practice is to try to prevent recurrences by using maintenance doses of digitalis for two to three months after the initial attack. If no recurrences are observed, digitalis treatment may be discontinued with the understanding that it will be reinstituted if the paroxysms recur. If, in spite of digitalis administration, the patient continues to have attacks, quinidine prophylaxis may be attempted with dosages starting at 100 mg. four times daily. This dose may be increased by 50 mg. per dose until either evidences of toxicity appear or the desired preventive effect is accomplished. *Although prevention of supraventricular tachycardia is often successfully accomplished with quinine, the treatment of choice in case of an attack is still digitalis.*

ANOXIC SPELLS

The "anoxic spells" represent real emergencies in the life of infants with cyanotic congenital heart disease.[5]

Etiology

Etiology of the attacks is unknown. It is assumed that they are associated with the sudden drop of arterial oxygen content. Sometimes they are initiated by severe crying. In other instances they always occur at certain times of day, specifically early in the morning. In a third group of patients the spells coincide with bowel movements. Interestingly enough, there is no correlation between exercise and the appearance of these spells. The attacks occur most commonly in the period between six months and two years of age. They are seldom observed in older children.

Symptoms and Signs

The "anoxic spells" usually start with irritability and fretfulness. Even if vigorous crying did not precipitate the attack, the infant usually starts crying at the onset. The cry may not be vigorous, but it is incessant and shrill. A few minutes later the respirations become more rapid and cyanosis increases. Shortly thereafter the infant is out of contact with his environment—his eyes roll upward, and occasionally convulsive twitches are noted. On examination, at this point, one is impressed with the deep cyanosis, the maximal dyspnea, tachycardia and the loss of consciousness. Otherwise the findings on physical examination are no different from what they were before the attack. There is no evidence of pulmonary or systemic congestion. The few laboratory tests that have been obtained during such a critical episode have been noncontributory except for evidences of a decrease in arterial oxygen content.

The duration of the attack is from a few minutes to several hours. It may terminate in cardiac arrest and death. Most commonly the dyspnea and tachycardia diminish, the color gradually improves, and the baby falls asleep for an hour or two and awakens in good condition.

Management

Management of the "anoxic spells" consists mainly in the administration of morphine sulfate subcutaneously in doses of about 1 mg. per 10 pounds of body weight. If the attack is severe, one half of this dose may be given intravenously. Oxygen by mask or in a tent is usually administered. Finally, it may prove beneficial to place the baby in a knee-chest position, either on the bed or on the parent's shoulder.

Prevention

Prevention of these attacks may be possible if they assume a predictable pattern both as to the time of occurrence and the premonitory

signs. In this case the mother can administer morphine suppositories by rectum at a certain time of the day and also could pick up the baby and hold it on her shoulder as soon as the signs of the characteristic fretfulness appear.

Prognosis

Prognosis of the individual attack may be fairly good, but the attack can terminate fatally. For this reason the appearance, persistence and progression of the number or severity of "anoxic spells" constitute clear-cut indications for surgical correction of the cyanotic congenital heart disease.

ACUTE CONGESTIVE FAILURE

Acute congestive failure in children is not nearly as common as it is in adults. It manifests itself principally as right-sided failure; evidence of left ventricular failure is often lacking.

Etiology

One specific cause of acute congestive failure in pediatrics, namely, paroxysmal tachycardia,[1] has been discussed in considerable detail. Other causes prevalent in the pediatric age group are "primary myocardial disease,"[2] acute glomerulonephritis[3] and acute rheumatic carditis.[6] Congenital heart disease seldom causes acute congestive failure; it is more likely to result in chronic congestion.

Symptoms and Signs

The presenting symptoms include irritability, anorexia, vomiting, shortness of breath, cough, cyanosis and edema. On physical examination, evidences of left-sided failure consist mainly in dyspnea, orthopnea, rales and gallop rhythm. Right ventricular failure is recognized most commonly by puffiness of the face and enlargement of the liver; distended neck veins, pitting edema and ascites are relatively rare. Both left- and right-sided failure are accompanied by cardiac enlargement and tachycardia. Paroxysmal nocturnal dyspnea is practically unknown in pediatrics.

Laboratory findings may include moderate polymorphonuclear leukocytosis, a mild degree of albuminuria with hyaline casts and minimal microscopic hematuria. The arm-to-tongue circulation time (Decholin or fluorescein) is prolonged. The venous pressure is elevated.

Radiologic examination always reveals an enlarged heart with rela-

tively feeble pulsations under the fluoroscopy screen. If the left ventricle is failing, the pulmonary vascular markings are accentuated and their outlines are blurred, especially near the hilum.

The *electrocardiogram* may show evidences of the underlying heart disease causing congestive failure, but is of no value in determining whether or not congestive failure is present.

Management

The management of congestive failure will depend to a great extent on its etiology. As a general rule, however, digitalis is the drug of choice in congestive failure of any etiology. The sensitivity of the patient to the glycoside, the expectation of success and the supportive measures may be very different, depending on the etiologic classification. Nevertheless digitalis should be given a trial in all cases of congestive failure.

"Primary myocardial disease," a syndrome encompassing at least five different etiologic entities,[2] responds often, though not invariably, in a dramatic fashion to digitalis therapy. A suitable dosage schedule has been outlined (Table 12). In addition to digitalis, oxygen, morphine and occasionally mercurial diuretics are recommended. It should be pointed out, however, that the therapeutic and toxic doses in the treatment of primary myocardial disease are rather close together, and great caution is to be exercised in the administration of the glycoside to these patients.

Congestive failure is one of the most serious complications of acute glomerulonephritis, an otherwise benign disease of childhood. In its most dramatic form it is characterized by the sudden appearance of pulmonary edema; in the less severe forms, cardiac enlargement, gallop rhythm and electrocardiograph T wave changes dominate the picture. The treatment, if instituted in time, is highly successful. It consists in decreasing the load on the circulation (lowering the blood volume, and using hypotensive drugs) and increasing the work-efficiency of the heart (digitalis). The dosage of digitalis is the one recommended before (Table 12). The blood volume may be lowered either by the use of tourniquets or by venesection, removing 100 to 250 ml. of blood. In terms of hypotensive drugs, magnesium sulfate (25 per cent solution) may be given intramuscularly in doses of 0.1 cc. per pound of body weight. More recently, Apresoline and Protoveratrine have been used with success (Table 12).

Congestive failure in acute rheumatic carditis has serious prognostic significance; the mortality in this condition may be as high as 50 per cent. All the anticongestive measures mentioned before have their place in the treatment of congestive failure in rheumatic carditis; digitalis, mercurials, oxygen and morphine are helpful. In a number of

institutions, within the past few years, the hormone treatment of acute carditis with congestive failure was found to be of life-saving importance. This therapeutic approach does not substitute for the judicious use of the anticongestive and antirheumatic measures used in the past. It does not, at this time, hold any definite promise for prevention of valvular lesions. In the views of many authorities on the subject, however, the hormones can and do save lives of many youngsters with fulminating rheumatic carditis with congestive failure. The experience in the past three years of the House of the Good Samaritan in Boston shows a striking lowering of the mortality of these children over the statistics for past years.

There is not enough experience available at this time to outline a detailed program for hormone treatment of rheumatic carditis; this type of treatment belongs to the institutions equipped with facilities for research on the subject. In broad outline, one may say that cortisone by mouth or ACTH parenterally may be used with equal success. Treatment should extend through two to three months, beginning with high doses (cortisone, 200 to 300 mg. a day; ACTH, 60 to 80 mg. a day) and tapering off gradually. The sodium chloride intake should be kept low, but added potassium chloride should be administered in the diet.

PERICARDIAL TAMPONADE

Pericardial tamponade represents a rare but significant cardiac emergency, the prompt recognition and treatment of which may prove life-saving.

Etiology

The etiology of pericardial effusion in children is most frequently rheumatic, although pyogenic, tuberculous and so-called idiopathic benign pericarditis do occur occasionally. Cardiac tamponade results if a large amount of pericardial effusion accumulates within a short time.

Symptoms and Signs

The patients complain of precordial pain, dry hacking cough and shortness of breath due to the pericardial effusion. On physical examination severe cardiac enlargement is noted. The neck veins show increased pulsations, the liver is enlarged, and the heart sounds are usually, though not invariably, distant. The heart rate is rapid. Murmurs may or may not be present, depending on the etiology of the effusion.

When the intrapericardial pressure, due to the accumulation of the effusion, becomes so high that the heart can no longer maintain an

adequate cardiac output, cardiac tamponade occurs. At this point the patient's symptoms attributed to the effusion are exaggerated; dyspnea becomes severe, and the child feels weak, complains of abdominal pain, and is often dysphagic. On examination, in the typical case, a drop in blood pressure is noted, pulsus paradoxus is evident, and signs of peripheral collapse appear. The patient is orthopneic and looks extremely ill. In the less typical case not all these symptoms are present, but neck vein pulsations and pulsus paradoxus are never lacking.

The *radiologic picture* characteristically shows a progressively enlarging, globular-shaped heart with feeble pulsations.

The *electrocardiogram* shows low voltages. S-T segment and T wave changes of varying degrees are noted at different stages of the disease.

Management

The management of pericardial tamponade consists in evacuation of the effusion. This, in many places where skilled surgical assistance is available, may readily be done by thoracotomy This avoids the possible danger of puncturing the myocardium or rupturing a coronary vessel. In most instances, however, pericardial paracentesis can be performed without undue risks. The approach should be the anterior one, well inside the apex beat, within the area of the cardiac dullness. If fluid is encountered, as much as possible should be removed, slowly. The improvement following removal of the fluid is quite dramatic.

However, not all pericardial effusions should be evacuated; as a matter of fact, most rheumatic effusions do well without paracentesis. The indication for pericardial tap is the presence of cardiac tamponade, not the effusion itself.

STOKES-ADAMS SYNDROME

Stokes-Adams syndrome is a complete ventricular standstill or extreme slowing occurring in patients with complete or partial heart block. It is an extremely rare condition in the pediatric age group.[4]

Etiology

Etiology of the heart block, underlying the Stokes-Adams syndrome, may be congenital or acquired. Congenital heart block may be an isolated cardiac finding or, more commonly, is associated with a ventricular septal defect. Acquired heart block may be the result of rheumatic or diphtheritic heart disease. Complete ventricular standstill is more likely to occur when a partial heart block develops into a complete block than when complete block is well established.

Symptoms and Signs

The syndrome, as originally described, consists of syncope and convulsions associated with slow heart beat. The child suddenly collapses, becomes pale and cyanotic, and continues to breathe, but no heart beat can be heard. If the asystole lasts more than a few seconds, anoxic twitchings and convulsions may ensue. If the ventricular pacemaker does not take over within a matter of two to three minutes, recovery is highly unlikely.

The *electrocardiogram* characteristically shows the P waves without any QRS complexes through several cycles.

Management

Management, most effectively, consists in prophylaxis rather than treatment. Oral administration of ephedrine in doses of 1.7 mg. per 10 pounds of body weight every six hours may prevent the recurrence of Stokes-Adams attacks. During the attack itself intravenous or intracardiac epinephrine has been the treatment of choice up until recently. Within the past year or so, Zoll[7] has described a simple artificial pacemaker, capable of stimulating the ventricles rhythmically and keeping up the cardiac output until the ventricular pacemaker can take over.

REFERENCES

1. Nadas, A. S., Daeschner, W. C., Roth, A., and Blumenthal, S. L.: Paroxysmal Tachycardia in Infants and Children. Pediatrics, 9:167, 1952.
2. Rosenbaum, H. D., Nadas, A. S., and Neuhauser, E. B. D.: Primary Myocardial Disease in Infancy and Childhood. Am. J. Dis. Child., 86:28, 1953.
3. Rubin, M. I., and Rapoport, M.: Cardiac Complications of Acute Hemorrhagic Nephritis. Am. J. Dis. Child., 55:244, 1938.
4. Stern, V. S.: Stokes-Adams Attacks in a Child. Brit. Heart J., 6:66, 1944.
5. Taussig, H. B.: Congenital Malformations of the Heart. New York, The Commonwealth Fund, 1947.
6. Walsh, B. J., and Sprague, H. B.: Character of Congestive Failure in Children with Active Rheumatic Fever. Am. J. Dis. Child., 61:1003, 1941.
7. Zoll, P. M.: Resuscitation of the Heart in Ventricular Standstill by External Electric Stimulation. New England J. Med., 247:768, 1952.

300 Longwood Avenue
Boston 15, Mass.

FLUID AND ELECTROLYTE MANAGENENT IN CHILDREN

DONALD E. PICKERING, M.D.

ROBERT W. WINTERS, M.D.

In this paper we wish to present a practical approach to fluid and electrolyte therapy in the pediatric patient. In compiling this material we have borrowed freely from the literature and have attempted to assimilate important physiologic concepts into an integrated plan of therapy without a detailed discussion of the basic physiologic information, which space limitations regrettably preclude.

To facilitate application of physiologic principles in individual problems, it is convenient to divide fluid therapy into three phases:[3, 9] (*a*) maintenance therapy, consisting of the basic day-to-day metabolic requirements; (*b*) deficit therapy, consisting in the restitution of previously incurred inordinate losses; and (*c*) replacement of contemporary losses, consisting in the repair of continuing losses. These phases are graphically presented in Figure 21.

MAINTENANCE THERAPY

Maintenance fluid and electrolyte requirements are grossly proportional to caloric expenditure and are best calculated on this basis. The caloric expenditure includes basal metabolism plus increments over basal metabolism brought about by activity, fever, growth, specific dynamic action of foodstuffs, and so forth. For purposes of determination of maintenance requirements, the caloric expenditure may be satisfactorily determined by estimating basal metabolism plus increments for fever and activity only; the other increments listed are necessary only in protracted parenteral fluid therapy.

From the Department of Pediatrics, University of California Medical Center, San Francisco.

A satisfactory estimate of basal expenditure may be obtained by reference to the standard height and weight tables (Table 13), provided clinical judgment is applied in estimating the proportions of physiologically active tissue.

TABLE 13. *Basal Metabolic Rate (Calories per 24 hours)*

WEIGHT (KG.)	GIRLS	BOYS	HEIGHT (CM.)	GIRLS	BOYS
3.0	136	150	**48**	134	..
4.0	205	210	**50**	159	..
5.0	274	270	**51**	..	160
6.0	336	330	**52**	186	175
7.0	395	390	**54**	214	200
8.0	448	445	**56**	246	225
9.0	496	495	**58**	278	260
10.0	541	545	**60**	309	300
11.0	582	590	**62**	341	315
12.0	620	625	**64**	373	360
13.0	655	665	**66**	404	390
14.0	687	700	**68**	433	420
15.0	718	725	**70**	462	450
16.0	747	750	**72**	489	480
17.0	775	780	**74**	515	510
18.0	802	810	**76**	539	534
19.0	827	840	**78**	560	565
20.0	852	870	**80**	581	590
22.0	898	910	**82**	601	612
24.0	942	980	**84**	619	635
26.0	984	1070	**86**	636	660
28.0	1025	1100	**88**	652	685
30.0	1083	1140	**90**	666	705
34.0	1137	1230	**94**	695	740
38.0	1207	1305	**98**	722	765
42.0	1274	1370	**100**	735	786
46.0	1338	1430	**105**	770	805
50.0	1399	1485	**115**	846	875
54.0	1458	1555	**125**	942	990
58.0	1516	1600	**135**	1057	1105
62.0	1572	1660	**145**	1208	1220
66.0	1626	1725	**155**	1386	1380
70.0	1679	1785	**165**	1544	1570

From F. B. Talbot,[29] with permission of W. F. Prior Company.

In febrile patients basal metabolism is increased by approximately 13 per cent for each degree (centigrade) of fever.[25] Increments for activity are assessed with more difficulty. With normal "roustabout" activity metabolic expenditure is increased about 100 per cent above basal; in patients at quiet bed rest the expenditure is increased by about 20 per cent. In bed patients receiving parenteral fluid therapy 20 to 40 per cent is usually a satisfactory starting point.

Thus, by determining basal caloric expenditure from the table and by adding appropriate values for fever and activity, caloric expenditure is conveniently calculated as follows:

Basal metabolism (Table 13)	Calories/24 hours
Increment for fever	13% basal/degree C.
Increment for activity	20–40% basal (see text)
Specific dynamic action	Approximately 15% on mixed diet (see text)
Growth	Approximately 5% basal (see text)

Calculation of Maintenance Fluid and Electrolyte Requirements from the Caloric Estimate

Average maintenance fluid and electrolyte requirements, expressed in cubic centimeters or milliequivalents per 100 calories expended, are shown in Table 14.

TABLE 14. *Maintenance Requirements*[9]

WATER	
Insensible water loss:	
Skin	30 cc./100 calories
Lungs	15 cc./100 calories*
Urine	50–60 cc./100 calories†
Stool	10 cc./100 calories
Minimal sweating	10 cc./100 calories
Total	115–125 cc./100 calories
ELECTROLYTE	
Sodium	2–3 mEq./100 calories
Chloride	1.5–2 mEq./100 calories
Potassium	2–3 mEq./100 calories
CALORIES AND PROTEIN	
Nonprotein calories	90 calories/100 calories
Protein calories	10 calories/100 calories
Nonprotein calories for protein sparing and prevention of ketosis	25 calories/100 calories

* In the absence of hyperpnea.

† Assumes good renal function, maximal protein-sparing action and no ketosis.

The total requirements of water, sodium, potassium and chloride for any patient may be calculated by multiplying the metabolic expenditure (in 100 calories) by the figures shown in Table 14. These amounts may then be translated into appropriate solutions by reference to Table 24, which shows the composition of commonly available solutions. The maintenance requirements should then be administered over the greater part of the twenty-four hour period for which they are intended.

This calculation of water and electrolyte requirements is satisfactory in the majority of cases, but requires modification in certain instances. In sodium-retaining conditions, e.g., edema, in the early postoperative period, and so on, sodium and chloride requirements should be reduced; while in salt-losing conditions, e.g., adrenal insufficiency and salt-wasting renal lesions, more may be necessary. In the presence of poor renal function, reduction or omission of potassium may be indicated.

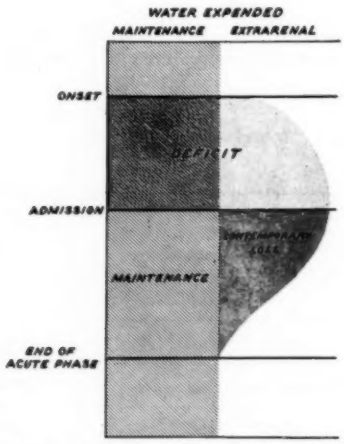

Fig. 21. A qualitative view of the three main phases of fluid and electrolyte therapy: maintenance, deficit, and replacement of contemporary losses.

Alteration of maintenance requirements is also necessary in patients who are sweating. Although the rate of such losses is not directly proportionate to caloric expenditure, it is convenient to regard sweating as a part of maintenance therapy. Figures listed in Table 14 cover only minimal losses of water and electrolyte through sweating. Losses considerably greater than these amounts may be encountered, especially in hot climates, and appropriate allowances must be made. Darrow and Pratt[9] estimate that approximately 50 ml. per 100 calories of sweat may be formed in a lightly clothed person in an environmental temperature of 85° to 90° F.

Calories

Energy requirements in acute illness and dehydration, because of short-lived carbohydrate reserves, are in large part met by the accelerated combustion of fat and protein with varying degrees of ketosis and neg-

ative nitrogen balance. While it is generally unnecessary to provide full parenteral caloric requirements in the acute phase of illness, provision of approximately 25 per cent of the estimated caloric needs as carbohydrate serves to minimize fat combustion and breakdown of tissue protein.

In chronic illness, when oral intake is precluded, or in malnourished persons undergoing acute illness more detailed attention must be given to the caloric problem. Under such circumstances recourse to caloric sources (Table 24) in addition to carbohydrates (alcohol, fat emulsions) is essential. Also, an attempt should be made to restore nitrogen equilibrium with protein hydrolysate.

DEFICIT THERAPY

This phase deals with the replacement of water and electrolyte losses incurred prior to the onset of definitive therapy. For estimating deficits in diarrhea, pyloric stenosis and diabetic acidosis, it is most convenient to use the data obtained from balance studies by previous authors. These data, shown in Table 15, are applicable to the *severe case*. Such cases of *severe* dehydration are clinically accompanied by loss of skin turgor, prostration, sunken and soft eyeballs, oliguria and shock, and occur with the acute loss of approximately 12 to 15 per cent of body weight. For milder cases appropriate reductions may be made. *Mild* dehydration is accompanied by lesser manifestations and may be evidenced by only minimal loss of skin turgor and a high urinary specific gravity. In such cases dehydration approximates 5 per cent of body weight.

TABLE 15. *Usual Deficits**

	WATER	SODIUM	CHLORIDE	POTASSIUM
	cc./kg.	mEq./kg.		
Diarrhea[8,11]	100–150	8–12	7–10	8–12
Pyloric stenosis[6,19]	150–200	12–17	15–19	10–14
Diabetic acidosis[1,10]	100–150	6–12	5–9	4–7

* Modified from references cited.

The therapeutic programs to be presented are formulated in terms of the average deficits in Table 15. In mild cases appropriate adjustment of data may be accomplished by using the degree of dehydration as a rough guide. Obviously, individual variation may require suitable alterations.

Time Sequence for Administration of Deficit Requirements

Figure 22 defines a time sequence for deficit repair therapy. The

recognition and treatment of shock (restoration of *circulatory integrity and renal function*) are of primary concern. The most effective treatment includes intravenous administration of salt-containing solutions and fresh whole blood or plasma.

Detailed attention should then be given to the replacement of extracellular and intracellular deficits. Complete repair of extracellular deficits can be effected within twenty-four hours, whereas complete replacement of intracellular electrolyte losses (potassium, phosphorus, magnesium) requires several days. For these purposes balanced multiple electrolyte solutions should be used.

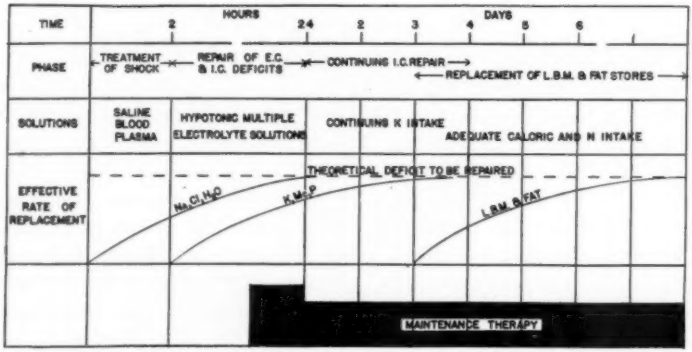

Fig. 22. Chronologic sequence of deficit therapy, showing the general time relations for the treatment of shock, the restoration of extracellular and intracellular deficits and the restoration of the lean body mass and the fat stores.

The third phase of deficit repair is concerned with the restoration of lean body mass and fat stores. This demands adequate caloric, protein, water, electrolyte and vitamin intakes. The time relationships of this phase have not been well worked out. In the uncomplicated case, restoration of the lean body mass and fat stores occurs when an adequate oral intake is provided and tolerated. However, in cases in which the oral route is precluded, attention must be given to parenteral provision of these materials.

REPLACEMENT OF CONTEMPORARY LOSSES

In addition to instituting a program of deficit repair and providing basic maintenance requirements, it is essential that provision be made to replace continuing extrarenal losses as they occur. The volume of these losses should be quantitated and their composition determined either by direct measurement or by reference to known average composition (Table 16). Replacement of these losses should then be made

by providing fluids approximating the volume and composition of the losses being sustained.

Gastrointestinal losses usually represent a mixture of secretions from several areas of the gut, and final composition must be approximated in each case. With this in mind, Cooke and Crowley[3] have introduced two solutions: a *gastric* solution, designed to replace losses primarily from the stomach, and an *intestinal* solution, designed to replace small bowel juices (Table 24).

TABLE 16. *Composition of Gastrointestinal Fluids*[3, 11, 22]

	SODIUM	POTASSIUM	HYDROGEN	CHLORIDE	HCO_3
	mEq./L.				
Gastric	60 (20–80)	15 (5–20)	50 (40–60)	125 (100–150)	.. ..
Biliary	130 (120–140)	10 (5–15)	.. ..	100 (80–120)	40 (30–50)
Pancreatic	130 (120–140)	10 (5–15)	.. ..	60 (40–80)	90 (70–110)
Small bowel	120 (100–140)	10 (5–15)	.. ..	110 (90–130)	30 (20–40)

	SODIUM	POTASSIUM	CHLORIDE	WATER
	mEq./kg./day			cc./kg./day
Diarrheal stools (severe)	3–6	3–5	2–4	50–70

Contemporary diarrheal losses in infants are often difficult to estimate. With severe diarrhea they approximate 60 ml. per kilogram per day, and in less severe cases 20 to 40 ml. per kilogram per day. Average composition of diarrheal stools is shown in Table 16.

Qualitative and quantitative replacement of contemporary losses should be made at sufficiently short intervals to avoid secondary changes. In actual practice the interval for evaluation of losses sustained, and their planned replacement, varies with severity and ranges from four to twelve hours. It may be desirable to anticipate losses and replace them as they occur.[3]

Continuing contemporary gastrointestinal losses can be minimized by withholding administration of any fluids or food by mouth. As Peters[23] has pointed out, the presence of fluid or food in the gut is a potent stimulus for the secretion of gastrointestinal fluids. If water is introduced through a tube, electrolyte will be secreted into the water col-

lection as part of the absorptive process. However, since the diseased gut often has lost its ability for absorption, the fluid will either be sequestered or lost through a suction tube or vomiting, with a resulting net loss of electrolyte.

ROUTES OF FLUID ADMINISTRATION

Available routes for administration of fluid and electrolyte requirements (deficit repair, maintenance and contemporary losses) include oral, rectal, hypodermoclysis, and intravenous. The oral route for administration of fluids is contraindicated when contemporary losses continue through the gastrointestinal tract (vomiting, diarrhea, obstruction). Rectal administration of fluids is unreliable.

The use of hypodermoclysis for the repair of extracellular deficits is not recommended, especially in dehydrated patients. This is particularly true when salt-poor solutions are being given. Such solutions are absorbed only after preliminary equilibration with extracellular fluid, in which there is an ingress of extracellular ions into the clysis collection. This preliminary equilibration process may be sufficient to further salt-deplete an already dehydrated patient and precipitate vascular collapse.[26, 30] Deaths from this mechanism have been recorded.

The intravenous route must be used in the treatment of shock and in the repair of extracellular deficits in all but the mildest cases.

Drip hypodermoclysis offers a convenient route for administration of ions destined for intracellular deficit repair (potassium, magnesium, phosphorus). The hypodermoclysis route may also be indicated in continued management of mild fluid and electrolyte disorders.

FLUID THERAPY IN SPECIFIC DISEASES

Therapy of specific disease states—including diarrhea, pyloric stenosis and diabetic acidosis—is presented in the following sections, together with some principles of preoperative and postoperative management. The general plan of therapy, as presented in Figure 22, will be followed.

Infantile Diarrhea[8, 11, 14]

The average deficits for infantile diarrhea are listed in Table 15, and one plan for repair of these deficits is shown in Table 17. Rapid intravenous infusion of the initial hydrating solution is necessary. This may be followed with transfusion of fresh whole blood or plasma, if indicated.

When circulatory and renal functions are adequately restored, repair of the remaining deficits may be started by the drip hypodermoclysis

TABLE 17. *Treatment Plan for Infantile Diarrhea*

PHASE	TIME	SOLUTIONS	AMOUNT	ROUTE	WATER	SODIUM	CHLORIDE	POTASSIUM
	Hours		cc./kg.		cc./kg.	mEq./kg.		
Treatment of shock	0–2	Ringer's lactate	10–20	IV	10–20	1.3–2.6	1.1–2.2	0
		Fresh whole blood or plasma	10–20	IV				
Repair of E.C. and I.C. deficits	2–8	5% or 10% CHO	40	IV	40	0	0	0
		Darrow's K-lactate	80	SQ (drip)	80	9.6	8.2	2.8
			Deficit repair: 1st day		130–140	10.9–12.2	9.3–12.2	2.8
Maintenance	8–24	See text						
Continuing repair of I.C. deficits	24–72	Potassium supplementation (3 mEq./kg.) in oral or parenteral fluids						
Restoration of lean body mass and fat stores		Adequate protein, caloric and vitamin intake						

of Darrow's potassium-lactate solution. This should be followed by provision of the daily maintenance requirements, with special attention to losses of water and electrolyte through sweating in hot climates.

In milder cases some authors recommend oral replacement of deficits by appropriate fluids. We prefer to routinely withhold all feedings in such cases and rely upon parenteral fluids, for fear of converting a mild case to a severe one.

After the acute phase fluid and electrolyte requirements may be given by mouth, provided there is no vomiting. With improvement and in the absence of symptoms or signs suggesting continuing diarrhea, viz., abdominal distention, anorexia, vomiting or voluminous watery stools, transition to a low fat, low caloric milk mix may be made. This must provide adequate maintenance water requirements, and should also be fortified with 2 to 3 mEq. per kilogram of potassium chloride per day.

Continuing major diarrhea contributes greatly to water and electrolyte losses. These losses may be approximated and repaired as already outlined. Appropriate bacteriologic studies and antibiotic therapy should be prescribed. If diarrhea continues, some provision must be made for caloric and protein maintenance.

Pyloric Stenosis and Vomiting

Fluid and electrolyte deficits in this disorder are listed in Table 15, and may be repaired by the plan outlined in Table 18. Once the diagnosis is established, oral feedings should be withheld to minimize vomiting and avoid further losses. In addition to the initial saline and glucose infusions, transfusion with fresh whole blood or plasma is indicated if the infant is in shock.

With restoration of satisfactory cardiorenal function, the remaining deficits are repaired by a slow hypodermoclysis of solution incorporating potassium chloride in amounts of 3 mEq. per kilogram. After repair of extracellular deficits and satisfactory institution of potassium repletion, operation may be performed.

Postoperatively, increasing fractions of maintenance fluids may be given by mouth (the remainder being given parenterally) followed by a gradual transition to a low fat formula. If vomiting develops, oral fluids should be discontinued and parenteral administration of all maintenance requirements resumed. Full potassium requirements should be given postoperatively.

Danowski and co-workers[6, 19] have clearly shown that a significant potassium depletion occurs in this condition and that early potassium administration accelerates the return of the body fluids to a more normal composition. To the extent that chemical equilibrium is more rapidly restored, the use of potassium may be expected to reduce mor-

TABLE 18. *Treatment Plan for Pyloric Stenosis*

PHASE	TIME	SOLUTIONS	AMOUNT	ROUTE	WATER	SODIUM	CHLORIDE	POTASSIUM
	Hours		cc./kg.		cc./kg.	MEq./kg.		
Treatment of shock	0–2	Isotonic saline	10–20	IV	10–20	1.5–3.0	1.5–3.0	0
		Fresh whole blood or plasma	10–20	IV				
Repair of E.C. and I.C. deficits	2–8	5% or 10% CHO	40–60	IV	40–60	0	0	0
		Mix: isotonic saline, 80 cc. 10% KCl, 2.3 cc.	80	SQ (drip)	80	12	15	3
			Deficit repair: 1st day		130–180	13.5–15.0	16.5–18.0	3
Maintenance	8–24	See text						
Continuing repair of I.C. deficits	24–72	Potassium supplementation (3 mEq./kg.) in oral or parenteral fluids						
Restoration of lean body mass and fat stores		Adequate protein, caloric and vitamin intake						

bidity and to provide some protection against development of manifest potassium deficiency if complications supervene.

Diabetic Acidosis[1, 15]

Table 15 lists the deficits of water and electrolyte which may be expected in a patient with moderately severe diabetic acidosis, and a plan for the repair of these deficits is outlined in Table 19.

Insulin. In addition to the requirements for water and electrolyte, attention must be given to the disordered carbohydrate metabolism, since, without control of the latter, adequate repletion of the electrolyte deficits is difficult. The recognition and treatment of the precipitating cause or causes of the acidosis, such as infection, trauma, emotional stress, starvation, and so forth, are of considerable importance. Such factors often play an important role in increasing the insulin requirement and hence contribute to continuing ketosis and electrolyte depletion.

Crystalline insulin should be principally relied upon. The initial insulin dose should be in accordance with the previous experience of the patient. If such information is not available, an initial dose of about 1 unit per kilogram may be given intramuscularly. In addition, a similar amount may be added to the initial intravenous infusion. Further insulin dosage should be gauged according to the response of the patient as judged by the clinical condition, the blood and urine sugars and the urinary ketones. The present tendency in many clinics is towards larger doses of insulin at more frequent intervals. Although such practice restores the carbohydrate metabolism more rapidly, it requires closer supervision of the patient to avoid serious hypoglycemic reactions.

Fluids. The initial parenteral fluids consist of hydration infusion which is slightly hypotonic and provides sodium, chloride and lactate in balanced proportions. This should be given rapidly and may be followed by a transfusion of whole blood or plasma if indicated.

The value of alkalinizing salts (such as sodium bicarbonate or lactate) has not been settled. *Large* doses of such salts (of the order of 10 mEq. per kilogram) are probably not indicated, since rapid restoration of the bicarbonate levels of the serum to normal (25 mEq. per liter) may induce an alkalosis. The most rational basis for the use of bicarbonate in the early phase stems from the observation of insulin resistance resulting from the acidosis per se.[18] In order to achieve a satisfactory restitution of the blood *p*H, the bicarbonate concentration should be raised initially *by* about 4 to 8 millimols per liter rather than *to* normal levels of 25 mEq. per liter. The dose of alkali required for this initial elevation cannot be accurately calculated or predicted, but it is of the

TABLE 19. *Treatment Plan for Diabetic Acidosis*

PHASE	TIME	SOLUTIONS	AMOUNT	ROUTE	WATER	SODIUM	CHLORIDE	POTASSIUM
	Hours		cc./kg.		cc./kg.	mEq./kg.		
Treatment of shock	0–2	Initial hydration solution (Table 24)	20–25	IV	20–25	2.0–2.5	1.2–1.5	..
		Fresh whole blood or plasma	10	IV				
Repair of E.C. and I.C. deficits	2–3	M/6 lactate	10	IV	10	1.7		
	2–8	5% or 10% CHO	40	IV	40			
		Diabetic deficit solution (Table 24)	50–70	SQ (drip)	50–70	5.0–7.0	3.0–4.2	2.3–3.2
			Deficit repair: 1st day		120–145	8.7–11.2	4.2–5.7	2.3–4.2
Maintenance	8–24	See text						
Continuing repair of I.C. deficits	24–72	Continuing K and P supplementation in oral or parenteral fluids						
Restoration of lean body mass and fat stores		Adequate protein, caloric and vitamin intake						

order of magnitude indicated in Table 19, and may be modified according to the individual patient and the serum chemistries.

A second objection to the administration of large quantities of alkali has to do with the large load of sodium which may be introduced. A hyponatremia is common in diabetic acidosis, but this does not give an accurate picture of the magnitude of salt depletion which may be present, since the reduction of the serum sodium concentration is in part referable to a dilution incident to the transfer of water from the cells due to the presence of an osmotically disturbing hyperglycemia.[27] Large amounts of sodium given early in diabetic acidosis predispose to the development of hypernatremia when the carbohydrate metabolism is restored.

These considerations should not deter one from the proper use of sodium-containing solutions in diabetic acidosis. Such solutions (initial hydration solution, Table 24) are definitely indicated in the treatment of shock and extracellular contraction deficits. However, additional large amounts of sodium in the form of alkali seem unnecessary and unwise.

After restoration of adequate renal and circulatory functions (shock therapy) and upon indications that carbohydrate metabolism is being restored, repletion of the intracellular deficits (potassium, phosphate) may be safely initiated. A simple solution suitable for this purpose is shown in Table 23 (diabetic deficit solution). Butler's solution[1] may also be used if available (Table 24). Provision of potassium and phosphate at this time, as well as guarding against hypokalemia and hypophosphatemia, helps in the repletion of the cellular losses and probably aids in the re-establishment of normal metabolic processes. Earlier administration of these electrolytes is not indicated, since their concentration in the blood may be initially elevated. It seems advisable to administer this solution by a drip hypodermoclysis.

The intravenous route, initially used for the treatment of shock, may be used in this phase for the provision of water and carbohydrate. Fructose rather than glucose appears to be the carbohydrate of choice in this period.[7]

Maintenance therapy and replacement of contemporary losses (if any) should follow the infusions of these solutions. These may be estimated by the methods already outlined. Continuing provision of potassium and phosphate should be made until the patient is able to take a regular diet.

PREOPERATIVE AND POSTOPERATIVE MANAGEMENT

Deficit Replacement

Deficits of sodium, chloride and water (and, preferably, intracellular

electrolytes as well) should be replaced preoperatively. Dehydrated infants are poor surgical risks and can ill afford compromise of their extracellular volume through operative blood loss. In the light of the common surgical practice to interdict fluids after midnight, part of the maintenance requirements should be given as clear fluids, parenterally, through the night. Calculation of maintenance requirements should take cognizance of the large losses of water which may accrue through the skin as the result of a long operation under heavy drapes and operating room lights. Blood loss should be treated as a contemporary loss and replaced during the procedure.

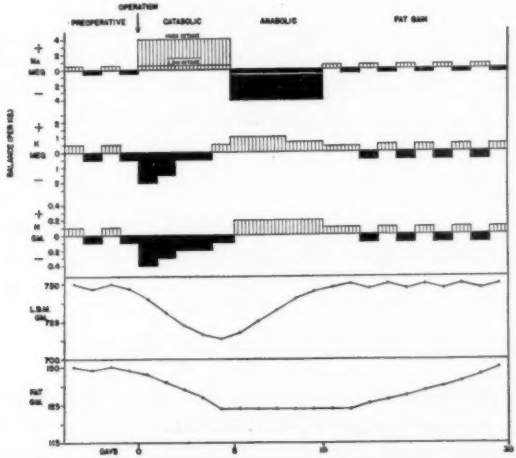

Fig. 23. A simplified scheme of the chief metabolic phenomena occurring in a previously well nourished patient after a major operation. The data are expressed on a per kilogram basis and are based on unpublished studies[33] in children of 6–8 years undergoing major intrathoracic surgery.

Postoperatively, one should take cognizance of the changing metabolism which occurs as the result of metabolic response to surgery.[21, 22] Figure 23 diagrams this in a qualitative way. In the initial period there are positive sodium balance (if any has been given) and negative potassium and nitrogen balances, along with signs of adrenal cortical stimulation. The degree and duration of this "catabolic" phase are variable, but seem to be governed by the magnitude of the operation. They are also conditioned to some extent by the age of the patient and to a considerable extent by the previous nutritional history. Younger children respond more vigorously than adults, while nutritionally depleted patients respond less vigorously than their well nourished counterparts.

This phase is succeeded by an "anabolic" one in which these metabolic phenomena are reversed. There is sodium diuresis and potassium and nitrogen storage—the latter presumably for the resynthesis of the lean body mass. Later in convalescence there is repletion of the fat stores as well, since in the catabolic phase they sustained the energy requirement.

Postoperatively, one should take note of these phenomena and alter maintenance requirements accordingly so as to provide less sodium and chloride in the catabolic phase. In addition, potassium should not be given until adequate cardiovascular and renal functions are restored. Thereafter, full requirements should be given.

In the presence of salt losses through suction, vomiting, and so on (contemporary loss), sodium administration is necessary and desirable. An undue fear of sodium administration postoperatively has often led to salt depletion or even the "low salt syndrome" by replacement of sodium-containing losses with glucose solutions.

SPECIFIC ELECTROLYTE DISTURBANCES

Specific electrolyte disturbances are categorically discussed without reference to specific disease. Reference to this section should be made in treating any disorder in which such disturbances would be found.

Potassium Depletion and Hypokalemia[2, 12]

In potassium depletion a number of etiologic factors are usually operative—most often a decreased intake together with a situation of stress which enhances output, with or without significant extrarenal losses. Hypokalemia may be manifest by weakness, paralysis, silent distention of the abdomen, dyspnea and cardiac signs, including cardiac failure, cardiac arrhythmias, widening of the pulse pressure and various electrocardiographic abnormalities. It is the atypical case which shows these signs unequivocally.

In diagnosis the electrocardiogram is helpful, but the characteristic tracings may sometimes be absent or incompletely developed. Coexistence of other electrolyte abnormalities would seem to accentuate or mask the signs and electrocardiographic manifestations. The rate at which the deficiency develops may also be of some importance in this regard. An analysis of the intake in the light of the probable need is valuable in the recognition and prevention of potassium depletion. Estimation of serum potassium concentration is most valuable in diagnosis, although occasionally it may be relatively normal in spite of a significant reduction of the total body potassium.

In infants the usual (and safe) dose for repair of potassium deficit is 3 mEq. per kilogram per day; in older children and adults, less may

TABLE 20. *Causes for Hypokalemia and Potassium Depletion*

I. INADEQUATE INTAKE
- a. Starvation
- b. Nonpotassium-containing parenteral fluids (especially sodium and glucose solutions)
- c. Ion exchange resins

II. EXTRARENAL LOSSES
- a. Gastrointestinal fluids
- b. Wound exudate

III. EXCESSIVE OUTPUT
- a. Stress
  - 1. Postoperative
  - 2. Burns (unless anuria is present)
  - 3. Acute medical diseases
- b. Hormones, drugs, etc.
  - 1. Cushing's syndrome
  - 2. DOCA, cortisone, ACTH
  - 3. Mercurial diuretics
- c. Renal disease
  - 1. Chronic nephritis with potassium wasting
  - 2. Diuretic phase of acute renal failure
  - 3. DeToni-Fanconi syndrome
- d. Acid-base disturbances
  - 1. Alkalosis, metabolic or respiratory
  - 2. Diabetic acidosis

IV. INTERNAL REDISTRIBUTION
- a. Familial periodic paralysis
- b. Recovery phase of diabetic acidosis

be used. This amount, if given parenterally, should be administered in not less than four to six hours, and preferably longer. Since the potassium deficits usually total about 10 mEq. per kilogram (Table 15), it is necessary to continue such intakes for several days to achieve full repletion.

In using parenteral potassium administration adequate circulatory and renal functions must be present, and potassium should not be administered in solutions in a concentration exceeding 40 mEq. per liter. Hypodermoclysis is the preferred route for administration of such solutions. Suitable preparations for parenteral administration of potassium may be found in Table 25.

Potassium Intoxication and Hyperkalemia

This condition is uncommon in pediatric practice and is usually confined to a situation in which the extracellular gain of potassium continues in the absence of efficient renal removal, e.g., acute renal failure with tissue destruction.

Iatrogenic potassium intoxication sometimes occurs when potassium is administered "therapeutically" under inappropriate physiologic conditions or in doses far in excess of those required. Conservative treatment of hyperkalemia has been aptly described by Elkinton.[13]

Transient hyperkalemia may occur after large transfusions of whole blood which has been stored for some time. Potassium levels may reach high levels in bank blood.[20] This is of especial importance in the exchange transfusion of erythroblastotic infants. It could also be of some importance if large volumes of such blood were used in the treatment of shock incident to such disorders as diabetic acidosis, in which the serum potassium level may be initially elevated.

Hyponatremia[17, 21]

Acute salt depletion ("low salt syndrome") is the most important cause of hyponatremia. It usually follows the rapid loss of salt with replacement by water. The signs and symptoms in this condition include apathy, confusion, tachycardia, hypotension, weakness, muscle cramps and, in the severe cases, convulsive seizures. Such symptoms probably

TABLE 21. *Causes of Hyponatremia*

I. ACUTE SALT DEPLETION ("LOW SALT SYNDROME")
- a. Acute external loss of sodium with water replacement
  - 1. Through the kidneys
    - (a) Excessive mercurial administration
    - (b) Base-wasting nephritis
    - (c) Adrenal cortical insufficiency
    - (d) Cerebral salt wasting
  - 2. Through the gastrointestinal tract
    - (a) Vomiting
    - (b) Diarrhea
    - (c) Fistulas
    - (d) Intestinal suction
  - 3. Through the skin
    - (a) Excessive sweating, particularly in unacclimatized persons
    - (b) Some patients with fibrocystic disease
  - 4. Other routes
    - (a) Delivery of large ascitic collection by paracentesis
    - (b) Subarachnoid ureteral anastomosis
- b. Internal sequestration of sodium with water replacement
  - 1. Burn edema
  - 2. Equilibration of nonsalt-containing clysis

II. ACUTE SODIUM DILUTION SYNDROME
- a. Hyperglycemia
  - 1. Diabetic acidosis
- b. Excessive ingestion or parenteral administration of nonsalt-containing fluids in the presence of pitressin or anuria.
- c. (?) Large nonsalt-containing enemas in megacolon

III. CHRONIC DILUTION HYPONATREMIA
- a. Chronic edematous conditions, particularly cardiac failure and nephrotic syndrome with restricted sodium intake

IV. OTHER
- a. Reduction of cellular osmolarity
  - 1. Malnourished patients, particularly with tuberculosis
  - 2. (?) Hypothyroidism
- b. (?) Osmoreceptor dysfunction—central nervous system disease

represent the combined effects of peripheral vascular collapse and water intoxication. The severity of symptoms seems to depend more upon the rate at which hyponatremia occurs than upon the absolute level of serum sodium.

In the presence of major symptoms, however, it is advisable to repair the sodium deficit rapidly. The amount of sodium to be given may be calculated by the following formula:[24]

$$\text{mEq. Na to be given} = (140 - \text{Na}_s) \times 0.6 \text{ Body Wt.}_{\text{kg.}}$$

where Na_s is the observed serum level of sodium of the patient. The total quantity of sodium to be administered should then be translated into an appropriate volume of a balanced hypertonic sodium solution (Table 24) and administered intravenously.

Salt depletion does not always necessarily call for specific therapy. Moderate salt depletion, commonly encountered in diarrhea, vomiting, and the like, may be adequately managed by the therapeutic programs already outlined.

Hypertonic sodium solutions may be indicated for treatment of seizures and other symptoms incident to acute sodium dilution even though such therapy may result in edema. Edema is not usually a serious deterrent to administration of such solutions, since, in the presence of adequate renal function, such edema will be rapidly mobilized. The acute sodium dilution sometimes seen in diabetic acidosis is adequately managed by the program already outlined and should not be treated with hypertonic saline solution.

The patient with chronic dilution hyponatremia is usually edematous and has often been maintained on a salt-free diet for some time. Therapy with hypertonic saline solution is generally contraindicated in such patients, seeming only to increase edema without restoring the sodium concentration deficit. However, an acute salt depletion superimposed upon chronic dilution hyponatremia definitely calls for provision of some extra salt.

Rarely there is a chronic lowering of the serum sodium apparently incident to cellular hypo-osmolarity. This is most often seen in patients who are malnourished, particularly those with bilateral, far advanced pulmonary disease. No specific therapy is indicated for these patients other than that directed against the primary disease.

Hypernatremia

This is an uncommon disorder, since the increase in the tonicity of the body fluids is a potent stimulus for thirst and increased water intake. It may develop, however, in patients who, for some reason, are unable

to communicate their desire for water (unconsciousness, infancy)[32] or in those rare persons who have organic or functional disorders of the thirst mechanism. With recognition of the significance of hypernatremia, therapy should consist in provision of adequate amounts of water.

TABLE 22. *Causes of Hypernatremia*

I. DEHYDRATION WITHOUT ACCESS TO WATER
  a. Unconscious patients
  b. Infants
  c. Organic or functional hypodipsia
II. EXCESSIVE INTAKE OR RETENTION OF SALT WITHOUT SUFFICIENT WATER
  a. Some patients with Cushing's syndrome
  b. DOCA intoxication
  c. Inhalation—certain sodium-containing mixtures
III. (?) OSMORECEPTOR DYSFUNCTION (? NEUROGENIC HYPERNATREMIA)
  a. Central nervous system disease
IV. DISTURBANCES OF CELLULAR OSMOLARITY
  a. Respiratory acidosis
  b. Immediate postconvulsive state

Of considerable importance is the observation that sodium-containing aerosol mixtures commonly in use in newborn nurseries may lead to hypernatremia and edema. Apparently the intake of sodium through inhalation exceeds the ability of excretion by these infants, with resulting accumulation of sodium in the body.

On rare occasions hypernatremia may accompany certain disorders of the central nervous system. This entity, called neurogenic hypernatremia,[5] *may* represent a specific disturbance of the osmoreceptor mechanism, although the evidence is not conclusive, and other causes of hypernatremia should be ruled out.

DISTURBANCES OF ACID-BASE EQUILIBRIUM

Physiologic Background

Major *p*H changes of the body fluids are tempered by the buffering action of two distinct mechanisms—the renal-respiratory system and the cellular-extracellular system. The renal-respiratory system, the better known of the two, tends to keep an optimal ratio of bicarbonate to carbon dioxide tension (pCO_2) through a balanced action upon (*a*) the bicarbonate concentration of the blood (through the action of the kidneys) and (*b*) the alveolar carbon dioxide tension (through action of the respiratory center and the lungs).

Primary distortions which lead to alteration in the *p*H of the blood may occur in either the bicarbonate concentration or the carbon dioxide tension. The system acts by altering the value of the other member of the ratio (compensation), thereby restoring the absolute value of the ratio to more nearly (but never completely) normal levels.

Acid-base disturbances may be classified according to which member

of the ratio is primarily affected—*respiratory disturbances* being the result of primary alteration of the carbon dioxide tension, while *metabolic disturbances* are the result of primary alterations in the bicarbonate concentration. Each of these groups may be further subdivided into an *alkalosis* when the *p*H is elevated above normal and an *acidosis* when it is below normal. Table 23 lists these disturbances, indicating some of the etiologic factors, the primary distortion and the type of compensation to the primary distortion which occurs.

TABLE 23. *Disturbances of Acid-Base Equilibrium*

$$pH = pK + \log \frac{[HCO_3^-]}{[p_{CO_2}]}$$

DISTURBANCE	PRIMARY DISTORTION	COMPENSATION		BLOOD pH	CO_2 CONTENT	INTRACELLULAR SODIUM	INTRACELLULAR POTASSIUM
		RENAL—RESPIRATORY	EXTRACELLULAR—CELLULAR				
RESPIRATORY ACIDOSIS PULMONARY DISEASE CNS DISEASE	INCREASED pCO_2	RENAL: CONSERVATION OF HCO_3^-	DECREASED H^+ TRANSFER	DECREASED	INCREASED	DECREASED	INCREASED
RESPIRATORY ALKALOSIS CNS DISEASE SALICYLISM FUNCTIONAL	DECREASED pCO_2	RENAL: EXCRETION OF HCO_3^-	INCREASED H^+ TRANSFER	INCREASED	DECREASED	INCREASED	DECREASED
METABOLIC ACIDOSIS STARVATION DIABETES RENAL DISEASE DIARRHEA SALICYLISM AMMONIUM CHLORIDE	DECREASED HCO_3^-	RESPIRATORY: DECREASED pCO_2	DECREASED H^+ TRANSFER	DECREASED	DECREASED	DECREASED	INCREASED
METABOLIC ALKALOSIS VOMITING (K DEFICIENCY)	INCREASED HCO_3^-	RESPIRATORY: INCREASED pCO_2	INCREASED H^+ TRANSFER (DECREASED K^+ TRANSFER)	INCREASED	INCREASED	INCREASED	DECREASED

The second buffer mechanism which serves to maintain the *p*H of the body fluids has only recently been elucidated. This system is primarily concerned with the exchange of ions between the cells and the extracellular fluid and may be called the extracellular-cellular system. The most rational theory[4] concerning the details of this system holds that under conditions of alkalosis there is an increased rate of transfer of hydrogen ions from the cells, while in conditions of acidosis there is a decreased rate of hydrogen transfer. The nature of the system, as it is presently visualized, is such that when hydrogen transfer is accelerated (alkalosis), sodium accumulates within the cells and potassium is lost from the cells in excess amounts; the opposite series of transfers occurs when hydrogen transport is inhibited (acidosis)—namely, an increased cellular potassium with a decreased cellular sodium. In potassium deficiency with alkalosis neither sodium nor hydrogen is effectively transported from the cells, owing to the low level of potassium in the extracellular fluid.

Practical Considerations

Rational diagnosis and treatment of acid-base disturbances must take

cognizance of the action of both the renal-respiratory and the cellular-extracellular systems.

Respiratory Acidosis and Alkalosis. In respiratory acidosis the pCO_2 is elevated and, as the result of renal compensation, the bicarbonate is elevated. The *p*H of the blood is still acid (Table 23). In respiratory alkalosis the pCO_2 is depressed as the primary disturbance and the renal compensation reduces the level of bicarbonate. In both disorders, changes occur in the cellular composition, as shown in Table 23, although these are generally not as marked as in metabolic disturbances.

In most of the respiratory disturbances little can be done for the definitive correction of the acid-base disorder other than those measures which alter the course of the underlying disease. However, it is important to provide adequate and appropriate fluid and electrolyte so that renal compensation can occur. This is particularly true in respiratory alkalosis (such as is encountered in salicylism), in which the kidney is called upon to excrete large amounts of bicarbonate. For such excretion to proceed efficiently an equivalent amount of sodium is required to match the bicarbonate anion in the urine. If sodium is not available, bicarbonate excretion (and hence effective renal compensation) may not proceed, and the urine may even become acid ("paradoxical aciduria" with systemic alkalosis).

Metabolic Acidosis. In metabolic acidosis there is a depressed level of bicarbonate through displacement by some other anion, and the *p*H is lowered. The respiratory compensation consists in hyperpnea, and the cellular-extracellular compensation consists in a retarded addition of hydrogen ion by the cells and an accelerated transfer of sodium (Table 23).

Correction of the acidosis depends upon the cause and the severity. For example, mild metabolic acidosis incident to the ketosis of starvation may be effectively managed by adequate provision of carbohydrate and does not call for large doses of alkalinizing salts. On the other hand, major symptoms ensuing from a severe acidosis may require "symptomatic treatment" with alkalinizing salts as well as attention to the primary cause of the acidosis (starvation, uncontrolled diabetes, diarrhea, and so on).

It is common practice in the treatment of metabolic acidosis to calculate the dose of alkali by some variant of the following equation:

$$\text{mEq. bicarbonate (or lactate) required} = (25 - CO_{2s}) \times 0.6 \text{ Body Wt.}_{kg.}$$

where CO_{2s} is the observed carbon dioxide content of the serum.

Several objections to this practice have been raised. It now seems likely that such large doses actually repair the intracellular sodium deficits of acidosis (Table 23) as well as the extracellular deficits of

bicarbonate. They appear to do so, furthermore, in a preferential manner[33] in that, when less than these amounts is given, the intracellular sodium deficits are repaired first and the acidosis persists. Since most cases of metabolic acidosis appear to have significant intracellular sodium deficits, these large doses are required. However, as Darrow and Pratt[10] have pointed out, if the intracellular deficits of sodium are less than anticipated (and they cannot be predicted), such large doses of bicarbonate could precipitate an alkalosis, since most of the bicarbonate would remain in the extracellular fluid.

A second objection to the use of these large amounts of alkali has to do with the finding that in some instances of diabetic acidosis[16,28] and in salicylate acidosis[33] the pCO_2 remains unduly low. In these conditions the respiratory center becomes relatively autonomous and continues to effect a hyperventilation even though such is not in the best interests of the body. If the bicarbonate concentration of the blood is then restored to normal (25 mEq. per liter), a respiratory alkalosis may be precipitated. This is more likely when large doses are given.

For these reasons it seems more reasonable to use smaller doses of alkali in the treatment of metabolic acidosis with more specific attention to the correction of the intracellular deficits. In practice, using the therapeutic programs outlined for diarrhea and diabetic acidosis, the acid-base balance may be effectively restored with minimal danger of alkalosis.

Metabolic Alkalosis. In metabolic alkalosis there is an elevation of the bicarbonate and the *p*H of the blood due, in most instances, to a loss of chloride. The urine is alkaline (unless the patient is salt-depleted and has "paradoxical aciduria"), and the respiratory compensation is manifested by a relative apnea. Parenthetically, it may be noted that the respiratory compensation for metabolic alkalosis is much less efficient than that for metabolic acidosis. The cellular-extracellular system also tempers the *p*H shift by increasing the rate of hydrogen ion transport from the cells (Table 23). As a result, potassium depletion may occur. The proper treatment, then, for metabolic alkalosis consists in the provision of adequate chloride and potassium; since salt-depletion often co-exists, sodium is also necessary.

TABLE 24. *Composition of Solutions (All Values per Liter)*

SOLUTION	CHO Gm.	N Gm.	Na mEq.	K mEq.	Cl mEq.	OTHERS	CAL.	ROUTE
5% Glucose in water	50						200	IV, SQ
10% Glucose in water	100						400	IV
5% Glucose in Saline	50		155		155		200	IV
10% Glucose in saline	100		155		155		400	IV
Isotonic saline			155		155			IV, SQ
Ringer's solution			148	4	158	Ca 6		IV, SQ
Ringer's lactate			127	4	110	Lactate 24 Ca3		IV
Gastric replacement	(100)*		63	17	150	NH_4 70		IV, SQ
Intestinal replacement	(100)*		138	12	100	Lactate 50		IV, SQ
M/6 Sodium lactate			167			Lactate 167		IV, SQ
Darrow's solution			120	35	105	Lactate 52		IV, SQ
Butler's multiple			55	23	45	P 12		IV
Electrolyte solution						Mg 5		
#1 Initial hydration sol.			100		60	Bicarb. (or lactate)		IV

#2 Diabetic deficit sol.			100	40	60	P 40 Lactate 40		SQ
3% saline solution			500		500			IV
#3 Hypertonic balanced salt			490		330	Lactate 160		IV
5% Amigen in 5% G-W	50	6	42	2	(44)		200†	IV
5% Amigen	50	6	42	2	(44)		550†	IV
5% G-W, 5% alcohol 10% Invert sugar	100						400	IV
5% Fructose	50						200	IV, SQ
10% Fructose	100						400	IV
5% or 10% Ethyl alcohol						Alcohol 50 gm. Alcohol 100 gm.	350 700	IV IV

* Available as electrolyte-10% G-W solutions from Baxter Company and to be used only by intravenous route.
† Indicates nonprotein calories.

#1, #2, #3—Table 23.

#1 INITIAL HYDRATION SOLUTION

Mix: 0.9% sodium chloride	400 cc.
Molar lactate	40 cc.
Pyrogen-free water	560 cc.
	1000 cc.

#2 DIABETIC DEFICIT SOLUTION

Mix: Initial hydration solution	1000 cc.
Potassium phosphate salts (Abbott)	15 cc.
	1015 cc.

#3 HYPEIC RTONBALANCED SALT

3% Saline	660 cc.
Molar lactate	160 cc.
Pyrogen-free water	180 cc.
	1000 cc.

TABLE 25. *Potassium Preparations*

I. POTASSIUM PHOSPHATE SALTS (ABBOTT)

KH_2PO_4	1.00 gm.
K_2HPO_4	4.59 gm.
Water	20 cc.

Each 20 cc. ampule contains 60 mEq. of potassium and 60 milliosmols of phosphorus, to be suitably diluted with other fluids (see text).

II. POTASSIUM CHLORIDE (10%):
Each cc. contains 1.3 mEq. of potassium and 1.3 mEq. of chloride.

Metabolic alkalosis often occurs in association with potassium deficiency. This alkalosis is often called "refractory alkalosis," since it cannot be repaired by sodium chloride, ammonium chloride or even hydrochloric acid, unless potassium is also given.

REFERENCES

1. Butler, A. M.: Diabetic Coma. New England J. Med., *243*:648, 1950.
2. Cooke, R. E.: The Role of Potassium in Fluid Therapy. Postgrad. Med., *14*: 257, 1953.
3. Cooke, R. E., and Crowley, L. G.: Replacement of Gastric and Intestinal Fluid Losses in Surgery. New England J. Med., *246*:637, 1952.
4. Cooke, R. E., and Segar, W. E.: A Proposed Mechanism of Extracellular Regulation of Muscle Composition. Yale J. Biol. & Med., *25*:83, 1952.
5. Cooper, I. S., and Crevier, P. H.: Neurogenic Hypernatremia and Hyperchloremia. J. Clin. Endocrinol., *12*:821, 1952.
6. Danowski, T. S., and others: Electrolyte and Nitrogen Balance Studies in Infants following the Cessation of Vomiting. Pediatrics, *5*:57, 1950.
7. Darragh, J. H., Womersley, R. A., and Meroney, W. H.: Fructose in the Treatment of Diabetic Ketosis. J. Clin. Investigation, *32*:562, 1953.
8. Darrow, D. C.: Therapeutic Measures Promoting Recovery from the Physiological Disturbances of Infantile Diarrhea. Pediatrics, *9*:519, 1952.
9. Darrow, D. C., and Pratt, E. L.: Fluid Therapy. Relation to Tissue Composition and the Expenditure of Water and Electrolyte. J.A.M.A., *143*:365, 432, 1950.
10. Darrow, D. C., and Pratt, E. L.: Retention of Water and Electrolyte during Recovery in a Patient with Diabetic Acidosis. J. Pediat., *41*:686, 1952.
11. Darrow, D. C., Pratt, E. L., Flett, J., Jr., Gamble, Alice H., and Wiese, H. F.: Disturbances of Water and Electrolytes in Infantile Diarrhea. Pediatrics, *3*: 129, 1949.
12. Elkinton, J. R., and Tarail, R.: The Present Status of Potassium Therapy. Am. J. Med., *9*:200, 1950.
13. Elkinton, J. R., Clark, J. K., Squires, R. D., Bluemle, L. W., Jr., and Crosley, A. P., Jr.: Treatment of Potassium Retention in Anuria with Cation Exchange Resin. Am. J. M. Sc., *220*:547, 1950.
14. Flett, J., Jr., Pratt, E. L., and Darrow, D. C.: Methods Used in Treatment of Diarrhea with Potassium and Sodium Salts. Pediatrics, *4*:604, 1949.
15. Guest, G. M.: Diabetic Coma: Metabolic Derangements and Principals for Corrective Therapy. Am. J. Med., *7*:630, 1949.
16. Kety, S. S., Polis, B. D., Nadler, C. S., and Schmidt, C. F.: The Blood Flow and Oxygen Consumption of the Human Brain in Diabetic Acidosis and Coma. J. Clin. Investigation, *27*:500, 1948.
17. Leiter, L., Weston, R. E., and Grossman, J.: The Low Sodium Syndrome: Its Origins and Varieties. Bull. New York Acad. Med., *29*:833, 1953.

18. Mackler, B., Lichtenstein, H., and Guest, G. M.: Effects of Ammonium Chloride Acidosis on Glucose Tolerance in Dogs. Am. J. Physiol., *168*:126, 1952.
19. Mateer, F. M., and others: The Use of Potassium Chloride in Preoperative Treatment of Pyloric Stenosis in Infants. Am. J. M. Sc., *221*:21, 1951.
20. Miller, G., McCord, A. B., Joose, H. A., and Clausen, S. W.: Studies of Serum Electrolyte Changes during Exchange Transfusion in Infants with Erythroblastosis Fetalis. Am. J. Dis. Child., *84*:637, 1952.
21. Moore, F. D.: Bodily Changes in Surgical Convalescence. I. The Normal Sequence—Observations and Interpretations. Ann. Surg., *137*:289, 1953.
22. Moore, F. D., and Ball, M. R.: The Metabolic Response to Surgery. Springfield, Ill., Charles C Thomas, 1952.
23. Peters, J. P.: The Structure of the Blood in Relation to Surgical Problems. Ann. Surg., *112*:490, 1940.
24. Peters, J. P.: Water Balance in Health and Disease, in Duncan, G. G., ed.: Diseases of Metabolism. 3rd ed. Philadelphia, W. B. Saunders Company, 1952, Chap. 6, p. 315.
25. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry. Baltimore, Williams & Wilkins Company, 1932, Vol. II, pp. 804–809.
26. Schechter, A. J.: Electrolyte and Volume Changes in Fluids Injected into the Peritoneal Cavity. Yale J. Biol. & Med., *4*:167, 1931.
27. Seldin, D. W., and Tarail, R.: Effect of Hypertonic Solutions on Metabolism and Excretion of Electrolytes. Am. J. Physiol., *159*:160, 1949.
28. Singer, R. B., and Hastings, A. B.: An Improved Method for the Estimation of Disturbances of the Acid-Base Balance of Human Blood. Medicine, *27*:223, 1948.
29. Talbot, F. B.: Basal Metabolism in Children, in Brenneman's Practice of Pediatrics. Hagerstown, Md., W. F. Prior Company, Inc., 1949, Chap. 22.
30. Webb, W., Lemmer, R. A., and Elman, R.: Absorption Rates. Electrolyte and Volume Changes Following Subcutaneous and Intraperitoneal Injections of Solutions Containing Salt, Glucose and Amino Acids. Surg., Gynec. & Obst., *91*:265, 1950.
31. Welt, L. G., and Seldin, D. W.: The Pathologic Physiology and Treatment of Edema. V. A. Tech. Bull. TB 10–69:1, 1951.
32. Welt, L. G., Seldin, D. W., Nelson, W. P., III, German, W. J., and Peters, J. P.: Role of the Central Nervous System in Metabolism of Electrolytes and Water. Arch. Int. Med., *90*:355, 1952.
33. Winters, R. W.: Unpublished studies.

University of California Hospital
San Francisco 22, Calif. (Dr. Pickering)

MANAGEMENT OF ACUTE PHASE OF THERMAL BURNS IN CHILDREN

ROBERT H. ALWAY, M.D.

Burns contribute a high percentage of the accident death toll in childhood. The mortality rate, however, inadequately depicts the physical, emotional and financial stress to a child and his family produced by a severe burn.

Better application of the knowledge gained regarding fluid, electrolyte and colloid shifts and losses should permit the greatest number of seriously burned children to survive. Although successful management of the immediate postburn period is no guarantee of eventual recovery, attention to other than antishock measures should increase the number of seriously burned children in optimal condition for early skin grafting.

ESTIMATION OF SEVERITY

A severe burn is one which is sufficient to produce shock or may later require grafting. The child under the age of six years with as little as 8 per cent partial thickness burn may require parenteral therapy. More than 15 per cent involvement may be equally serious in the child aged six to twelve years. These are in contrast to greater than 20 per cent area of equal seriousness in the adult. The depth of involvement is important in that a considerably smaller area of full thickness (third degree) burn may be equally serious. Flame burns are more apt to produce deep involvement than are hot liquid scalds. More anemia, both early and late, seems to follow third degree burns of any extent.

Correct estimation of the extent and depth of burn injury is difficult when the patient is first seen. Usually the area is exaggerated and the depth underestimated. The extent of the burn, so far as this affects therapy, may be calculated satisfactorily from a modification of Berkow's[1] and Wallace's[6] suggestions.

Head	9%
Neck	1%
Arms, each	9%
Trunk, front	18%
back	18%
Genitalia	1%
Legs, each (including buttocks)	18%

Allow relatively more for the head (almost two times) and less for the legs (about one half) in children under two years. Finally, in estimating severity the time elapsed from burn insult is important.

NATURAL HISTORY OF SEVERE BURNS

The natural history of burns may be divided roughly into three periods:

Phase I: the first forty-eight to seventy-two hours following the burn; marked by shock and edema

Phase II: third through the tenth day approximately; may be marked by water intoxication, hyponatremia

Phase III: after the tenth day with slough, sepsis and starvation

Phase I

In the twenty-four to forty-eight hours after a burn there is a relentless expansion of the extracellular fluid space, in the burned area as well as the rest of the body. Without replacement measures adequate in rate, volume and composition, not only may shock develop, but also the patient's later course may be prejudiced. This "loss" into an abnormal third space (burn edema) may equal a 50 per cent increase in extracellular fluid volume within a few hours. The associated decrease in effective circulating volume may be exaggerated by loss from the burn surface and further complicated by a variable degree of decreased red blood cell circulating volume. This loss is greatest in full thickness burns. This occurs early from hemolysis and stasis and later from decreased regeneration and surface loss from granulation tissue. This dislocation of extracellular fluid being most rapid in the first eight to twelve hours, early rapid replacement or maintenance of an adequate circulating volume is essential.

Renal function may be altered as a result of several factors. With delayed or inadequate replacement therapy effective renal plasma flow may decrease to one tenth or less of normal within minutes to a few hours after a burn. The usual response to severe stress results in sodium and water retention and failure to conserve potassium. Finally, morphine or barbiturate therapy may lead to an increase in antidiuretic hormones, an inability to excrete excess water and signs and symptoms of water intoxication.

Phase II

The "toxic" picture frequently presented by the severely burned subject between the fourth and tenth days is poorly understood, and accordingly there has been an unsatisfactory lowering of the mortality in this phase. "Adrenal exhaustion" does not adequately explain the picture, nor has adrenal cortical replacement therapy satisfactorily handled it. Hyponatremia may be noted. Water intoxication may be suggested by salivation, vomiting, twitching and convulsions. The older child may complain of headache or blurred vision.

Phase III

The third phase in the course of severe burns is marked by separation of eschars. This may be complicated by infection. Liedberg and co-workers[4] recently restressed the relative importance of group A beta-hemolytic streptococcal infections in the failure of skin grafting. In their experience staphylococci, pseudomonas, proteus and the coli-aerogenes group are not apparently of like significance. Infection may not only delay satisfactory closure of the burn wound, but may also interfere with adequate correction of hypoproteinemia and anemia.

TREATMENT

A formula for therapy connotes a degree of precision which, however, is not real. A rule-of-thumb approach is as apt to mislead. Despite the diverse opinions and multiple therapeutic regimens espoused, it should be possible to proceed on some general principles concerning three major obstacles to the recovery of the severely burned patient. These obstacles are shock, sepsis, starvation. Measures taken in the first forty-eight hours are not merely to restore or maintain an adequate circulation, but equally should be designed to carry the patient into the second and third phases in optimal condition. This is to facilitate early closure of the burn wound. Electrolytes, particularly sodium, water and colloids, including whole blood, all may be essential. Emphasis on one, relatively minimizing others, may permit survival through the first postburn phase, but with an unnecessary handicap.

The treatment of severely burned children based on surface area involved has not been satisfactory in our hands. We have used a modification of Cope's[2] suggestions in which the upper limit of deficit therapy is based on anticipated expansion of the extracellular fluid space and modified by the hourly urine output.

Fluid Therapy in Phase I

The amount of fluids required in the first forty-eight hours after a burn may be estimated as follows:

A. To cover expanding extracellular fluid space—volume in milliliters equivalent to not over 10 per cent of the patient's admission weight in kilograms;
B. To provide for surface loss from the burn—about 50 ml. per 1 per cent of burn area;
C. To cover the normal daily requirements for insensible loss and urine volume—200 ml. of water per kilogram per forty-eight hours and 10 to 15 gm. of glucose solution per kilogram for the same period. This amount may be divided in four equal volumes given in each twelve hour period intravenously.

The sum of quantities A and B, divided equally between colloid and electrolyte solutions, may be given intravenously, one half in the first eight hours after the burn, one fourth in the second and third eight hours, and one fourth in the second twenty-four hours. This volume of fluid may be too much or too little. More should be given only if the hourly urine volume decreases below 10 to 20 ml. or with other manifestations of inadequate treatment: rising pulse, hematocrit over 60 per cent, hypotension, and so on. *Colloid* may be given as plasma, Dextran or blood. The last may be given in amounts equivalent to 2 to 4 per cent of the patient's body weight in the first twenty-four hours. Blood should be used with a known or presumed full thickness burn, as in extensive fire burns. *Electrolytes* should be given as balanced salt solution: two parts of 5 per cent glucose in normal saline solution to one part sixth-normal sodium lactate solution rather than "unphysiologic" saline solution containing a relative excess of chloride.

As soon as the child is out of shock and not vomiting, oral intake may be encouraged. Salt solution may be tolerated if offered repeatedly in small amounts. A palatable solution may be made by adding 3 gm. (1 teaspoonful) of sodium chloride and 1.5 gm. (two-thirds teaspoonful) of sodium bicarbonate to one quart of iced water. Parenteral therapy should be curtailed proportionally to the retained oral intake. Tap water should not be offered in the first forty-eight hours unless dry oral mucosa, severe thirst or a serum sodium over 138 mEq. per liter is noted.

Hourly Urine Volume

The urine output is a reasonably satisfactory measure of the adequacy of fluid therapy in the acute postburn period. An indwelling catheter will facilitate accurate urine collection. An output of 30 to 50 ml. per hour is within safe limits. Continued hourly volumes over 80 ml. imply too much fluids, while volumes under 10 to 20 ml. should be investigated. A low hourly output usually means inadequate fluids to keep up with the expanding extracellular fluid space and consequently a decreased circulating volume. It may, though, result from renal damage. The

problem may be resolved by water loading. Give 25 ml. per kilogram of 5 per cent glucose in water intravenously in forty-five to sixty minutes. If no change in urine flow follows, renal tubular damage may be present. Continued increased fluid intake might then be disastrous. An increased flow subsequent to the water load is an indication for more vigorous treatment.

Local Therapy

Strict aseptic technique should be maintained at all times by all personnel until the burn wound is healed. Cover the patient with a clean sheet until general supportive measures have been started. After obvious dirt has been removed with a liquid detergent and the burned area flushed with warm saline solution, the less done the better. No local medication is probably the best general rule. Burned extremities should be elevated and immobilized with joints in a position of function. Open or closed handling of the burn wound will depend on the extent and location of the burn and the facilities available.

Additional Orders for Acute Phase Treatment

The following should be restressed or done in addition to those points already discussed:

Maintain strict isolation and aseptic technique. Type and crossmatch blood on admission. Record the hourly urine volume. Administer tetanus antitoxin, 1500 units, and procaine penicillin, 300,000 units daily intramuscularly, or its equivalent.

Oral feeding is ill tolerated in the acute phase. Children, however, usually will accept hard candy and sweetened carbonated drinks quite early. This should be encouraged.

SUMMARY

In children shock may follow considerably less extensive burns than in adults. Because of the rapidity of the development of shock, therapy should be started immediately in a child under six years of age with over 8 per cent of burned area. A plan of therapy based on the anticipated expansion of the extracellular fluid space has been satisfactory in our experience, being remarkably free of secondary complications therapeutically induced. The use of whole blood, sodium without chloride excess and little or no electrolyte-free water in the acute phase are emphasized. Rigid adherence to aseptic technique and isolation plus the prophylactic use of penicillin should facilitate early closure of the burn wound and a more rapid recovery.

REFERENCES

1. Berkow, S. G.: A Method of Estimating the Extensiveness of Lesions (Burns and Scalds) Based on Surface Area Proportions. Arch. Surg., 8:138, 1924.
2. Cope, O., and Moore, F. D.: The Redistribution of Body Water and the Fluid Therapy of the Burned Patient. Ann. Surg., 126:1010, 1947.
3. Liedberg, N. C-F., Kuhn, L. R., Barnes, B. A., Reiss, E., and Amspacher, W. H.: Infection in Burns. I. The Problem and Evaluation of Therapy. Surg., Obst. & Gynec., 98:535, 1954.
4. Liedberg, N. C-F., Kuhn, L. R., Barnes, B. A., Reiss, E., and Amspacher, W. H.: Infection in Burns. II. The Pathogenicity of Streptococci. Surg., Obst., & Gynec., 98:693, 1954.
5. Moyer, C. A.: Recent Advances in Chemical Supportive Therapy of Thermal Injury. Texas State J. Med., 45:635, 1949.
6. Wallace, A. B.: The Exposure Treatment of Burns. Lancet, 1:501, 1951.

4200 East 9th Avenue
Denver 20, Colorado

INTESTINAL OBSTRUCTION IN EARLY INFANCY

TAGUE C. CHISHOLM, M.D.

BERNARD J. SPENCER, M.D.

OSWALD S. WYATT, M.D.

Although many young infants with intestinal obstruction are today successfully treated, there still remain too large a number who die either because the condition is unrecognized or is detected too late or the management is injudicious. It is the purpose of this article to review the more common causes of intestinal obstruction in infancy with an eye to *early recognition* and *appropriate prompt management* in the hope that more children may live.

Babies with intestinal obstruction have an extremely narrow margin of safety. With persistent vomiting they rapidly become dehydrated; with dilated loops of bowel their electrolytes quickly plunge into imbalance; vomiting and distention are soon attended by disturbed thoracic physiology with either aspiration pneumonia from the one or compression atelectasis and restricted pulmonary ventilation from the other. Since the bacterial flora is incompletely established in the oropharynx, the tracheobronchial tree and gastrointestinal tract of young infants, the least virulent organism can constitute a threat to life. The renal flow in the newborn, at best, is infinitesimally small, and intestinal obstruction further jeopardizes the adequacy of renal function. The thermostatic control mechanism of small infants is so labile that excessive hypothermia and hyperthermia too often quickly accompany intestinal obstruction with unhappy consequences. Because infants have such a narrow margin of safety, *early recognition* and *appropriate prompt management* of intestinal obstruction are mandatory!

Not too many years ago the philosophy prevailed that one anomaly probably meant several others and that surgical efforts to relieve in-

testinal obstruction in infants were unwarranted heroics. This has not been substantiated by experience; every infant is worth trying to save. Even prematurity of 2 or 3 pounds is not a contraindication to extensive corrective procedures.

Mortality and morbidity percentages have shown marked improvement in the past two decades. Several factors are responsible: improved anesthetic agents with or without infant plastic endotracheal tubes; the free use of enduring cut-downs with polyethylene tubing instead of metal cannulas; an increased knowledge of the electrolytic needs of infants; whole blood transfusions, plasma and salt-poor albumin; the liberal use of broad-spectrum antibiotics before infection has set in; supplementary vitamins; infant incubators with controlled temperature, humidity and oxygen inflow. Yet the existing mortality and morbidity figures remain too high; they can be further lowered by *early recognition* and *prompt attention to detailed care*. These two arms encircling the successful management of intestinal obstruction in infants need further strengthening.

ATRESIA OF ESOPHAGUS WITH OR WITHOUT TRACHEO-ESOPHAGEAL FISTULA

Although this embryologic anomaly occurs relatively infrequently (1 in 14,000 deliveries), its early recognition is paramount to its successful management. Dehydration, aspiration pneumonia, elevation or depression of normal temperature, protein depletion, oliguria, poor wound healing and metabolic exhaustion quickly attend the overlooked case.

Some years ago Vogt[15] classified these high esophageal obstructions in a simple fashion (Fig. 24). Type III b is the most frequent and accounts for over 80 per cent of the entire group. With this diagram in mind the symptoms are easily understood.

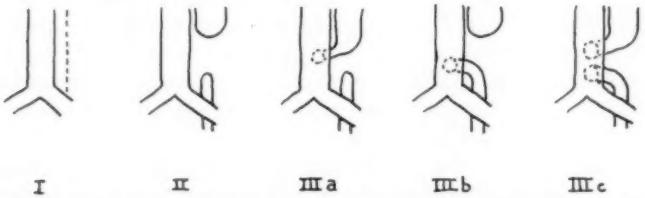

Fig. 24. Schematic drawing of Vogt's classification of atresias of esophagus with and without tracheo-esophageal fistula. Note that type III b is the most common.

Such babies swallow saliva, which soon fills the blind proximal pouch. Hence excess mucus requiring frequent suctioning is the first symptom. Not all mucus is regurgitated out the mouth; some is aspirated. Hence bouts of cyanosis with dyspnea are seen early. This should be enough

to raise the suspicion of the diagnosis, but should such a baby be fed, all liquids are promptly regurgitated without reaching the stomach. Fancy roentgenograms are unnecessary, and the mere inability to pass a soft rubber number 8 French catheter into the stomach is nearly pathognomonic. Instilling lipiodol helps define the anatomic level of the pouch (Fig. 25), but barium should *never* be given. Aspiration barium pneumonia can be intractable and fatal.

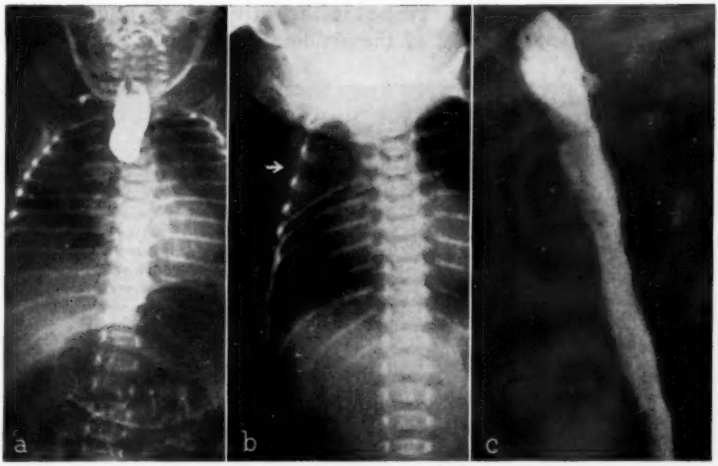

Fig. 25. *a*, Lipiodol esophagogram demonstrating blind proximal pouch. *b*, Chest roentgenogram taken 24 hours after surgical correction of type III b tracheo-esophageal fistula. Note 4 ribs partially resected. *c*, One year postoperative esophagogram done with barium. Note barely discernible site of primary anastomosis.

Prompt surgical intervention follows early recognition. The technical details have been well described by Ladd,[6] Levin,[10] Haight,[4] Swenson[13] and Gross.[3] Not too much stress can be laid on the equal importance of minute detailed postoperative care and experienced constant nursing supervision.

DIAPHRAGMATIC HERNIA

Diaphragmatic hernia is not too uncommon an anomaly (1 in 6000 deliveries). Newspapers are always describing a baby being flown from hither to yon to have his "upside-down stomach" fixed. The implied urgency is a real one, for the margin of safety is indeed narrow.

Since 80 to 85 per cent of diaphragmatic hernias occur on the left side posterolaterally, it is important that one have a sharply defined clinical picture in mind in order to diagnose the condition promptly.

Many of these babies are born with a small hernial orifice in the diaphragm, both lungs well expanded, and the entire abdominal viscera within the abdomen. With the ingestion of gas, normal peristalsis and intermittent negative intrathoracic pressure the viscera rapidly migrate into the left chest. At first the left lung is compressed, and the wee one shows mild dyspnea. As the left chest becomes filled with increasing loops of bowel, the left lung becomes atelectatic, the heart shifts towards the right, and the infant displays progressive dyspnea and cyanosis. Finally the heart is pushed to the extreme right, only the right lower lung is aerated, most of the abdominal viscera become trapped

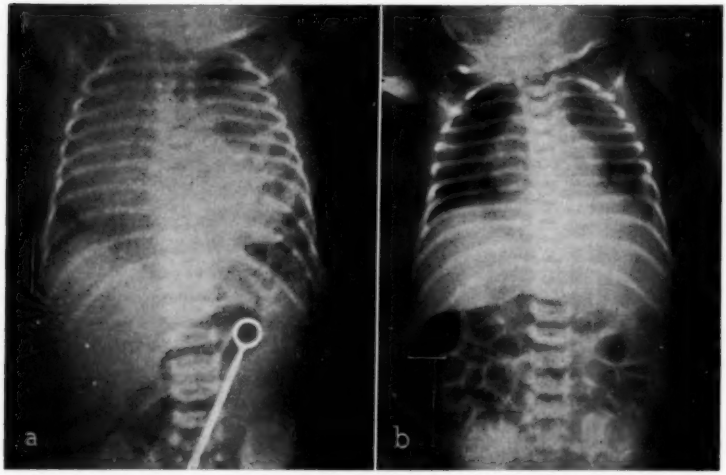

Fig. 26. *a*, Preoperative chest roentgenogram of diaphragmatic hernia. Note the loops of bowel filling the left chest, the compression of both lungs, the displacement of the heart, and the scanty intestinal gas pattern in the abdomen. *b*, Postoperative chest roentgenogram of diaphragmatic hernia taken 5 days after corrective surgery.

in the left chest, the abdomen is scaphoid, and the infant rapidly becomes critically ill. On physical examination (1) the heart sounds are on the right, (2) peristalsis is heard in the left chest, and (3) the abdomen is concave with no loops of bowel to furnish the usual pot-shaped belly of the newborn. With these three cardinal findings a diaphragmatic hernia is present until proved otherwise, and prompt emergency management is essential.

Roentgenograms (Fig. 26) merely confirm the clinical impression. Barium swallows are not necessary and are dangerous; the esophageal barium column laboriously turns at the diaphragmatic angle to enter the upside-down stomach with difficulty; aspiration can easily ensue.

While going to the operating room, the infant should be given ox-

ygen; machine suction must be available; and holding the infant in Fowler's position does afford considerable relief to pulmonary ventilation. A left rectus incision furnishes rapid and easy access to the usually affected side. By exercising traction on the sigmoid, the entire large bowel, small bowel, stomach, spleen, left lobe of the liver, and occasionally the left kidney are delivered from the chest in that sequence. Immediately the anesthetist's burden is eased and oxygenation of the baby is facilitated.

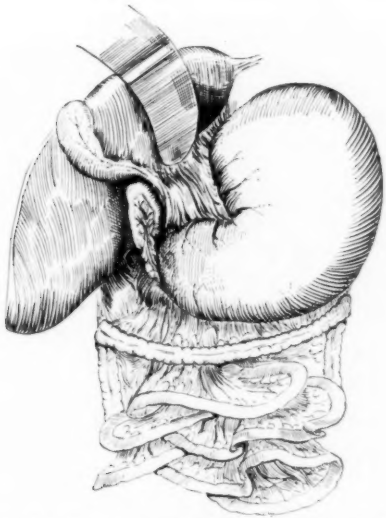

Fig. 27. Schematic drawing of complication following repair of diaphragmatic hernia. The unattached spleen on a long pedicle became lodged in the foramen of Winslow and obstructed the pylorus. Splenectomy was necessary.

The techniques of the repair of diaphragmatic hernia are well outlined by Gross.[3] The postoperative complications are few. One recently encountered by us is illustrated in Figure 27. The unattached spleen on a long pedicle became lodged in the foramen of Winslow, obstructed the duodenum and required subsequent splenectomy.

The most important issues are the *early recognition* of the not too uncommon anomaly and its *urgent surgical correction.*

NORMAL GAS PATTERN OF SMALL AND LARGE INTESTINES

For the early recognition of intestinal obstruction below the diaphragm a full knowledge of the pattern of the motility of ingested air

through the gastrointestinal tract of newborn infants is absolutely essential. Too little credit is given to Wasch and Marck[16] for studying this problem in the full term and mature baby. Too little attention has been given to the subject in premature and immature newborns.

As soon as a normal, full term, mature baby is delivered, it starts to ingest air. Within minutes to a couple of hours air has passed through the stomach and duodenum; after a few hours air is well down into the jejunum and ileum; usually by twelve hours air has passed into the colon; and by fifteen to eighteen hours gas ordinarily has reached the rectum.

Any full term mature baby with vomiting, abdominal distention, whether generalized or epigastric, intestinal patterning through the abdominal wall, or dyspnea with cyanosis should promptly have an x-ray picture taken of the chest and abdomen. Deviations from the normal intestinal gas pattern from whatever cause are at once visible. Urgent appropriate surgical intervention can immediately be instituted.

X-ray pictures of the abdomen of premature and immature newborns, on the other hand, are not necessarily nearly so informative. In this area our knowledge is scanty, but we have seen such youngsters mimic clinically and radiologically intestinal obstruction who have no anatomically demonstrable lesion at operation.

NORMAL PATTERN OF DEFECATION

No one who has dealt to any extent with healthy newborn babies has not come to admire the beautiful green color and the thick molasses consistency of normal meconium. Once a baby has passed such material, all hasten to admire this natural performance. Then again, no one who has watched newborn babies, even a little, has not been surprised at either the promptness or the tardiness with which this natural act is accomplished. For a few it is before or during labor; for some it is shortly after birth; and for most it occurs within the first six to twelve hours of extrauterine existence. An occasional newborn fails to defecate for eighteen to twenty-four hours and for this seems none the worse.

We want to call especial attention to the experience that no meconium stool for the first twelve hours is accepted without question; this constitutes a solid green signal light of approval. But no meconium stool after twelve to eighteen hours is a warning; the signal light has turned to flashing orange. No meconium bowel movement after twenty-four hours demands careful scrutiny; the signal light has become a steady red.

With intestinal obstruction in infancy an abnormal pattern of me-

conial defecation may be the first evidence of trouble. A thorough evaluation of the patient in whom no meconium appears during the first twenty-four hours of life is necessary to the *early recognition* and *prompt surgical correction* of any cause of intestinal obstruction.

ATRESIA OF INTESTINES

Atresia of the intestine is by no means a rare cause of bowel obstruction in infancy (1 in 8000 deliveries). No single physician sees many in a year's practice of obstetrics or pediatrics; yet when one does appear, it must be recognized early and treated with dispatch if it is to be rescued. Such atresias may occur anywhere from mouth to anus, but the vast majority are either duodenal (with high intestinal obstruction) or ileal (with low intestinal obstruction). In order to reduce further the existing mortality for these conditions, one must have a clear-cut clinical picture in mind in order to detect them early.

In all atresias of the intestines there are *no meconium stools*. The importance of this fact has been embellished. When one goose egg (0) appears on an infant's twenty-four hour stool chart, there is no cause for alarm; two goose eggs (00) on the defecation sheet require immediate investigation; and three goose eggs (000) represent neglect; the infant's narrow margin of safety has been jeopardized. Although the situation is not hopeless after the third day of obstruction, it is, to say the least, considerably worsened.

With atresia of the duodenum, vomiting comes into the picture early. Such vomitus usually is bile-stained. Bile-stained emeses do not attend intracranial damage or sepsis or congenital heart disease; bile-stained emeses are a signal warning of first import. With atresia of the duodenum, inspection of the abdomen ordinarily shows a distended or full epigastrium and an empty or concave lower abdomen. If the baby is inspected soon after an emesis, however, this may not be apparent. Simply placing a soft number 8 French rubber catheter into the stomach and pumping in 100 to 150 cc. of air will demonstrate its validity or absence. Simultaneously a scout x-ray film of the abdomen will confirm the clinical observation of a dilated stomach and duodenum with no gas beyond (Fig. 28).

With atresia of the ileum, vomiting comes into the picture much later—on the second, third or fourth day of life. With atresias low in the intestines the earliest warning is frequently *no meconium stools* on the second day of life. Slowly the abdomen becomes distended. Some regurgitation is observed, but not projectile vomiting with bile. A little later intestinal patterning is noted through the distended, thin abdominal wall. By this time bile-stained regurgitation is definite,

and later vomiting becomes fecal in odor and appearance. Cyanosis, dyspnea and aspiration are complications which attend prolonged obstruction, with distention, weight loss, dehydration and malnutrition (Fig. 29).

Early detection of an atresia causing intestinal obstruction is the cornerstone for a successful outcome. Upon this must be placed prompt, judicious surgical intervention. Between the diagnosis and the operation several details have considerable importance. Among them are (1) a careful gastric lavage to minimize the hazard of aspiration under general

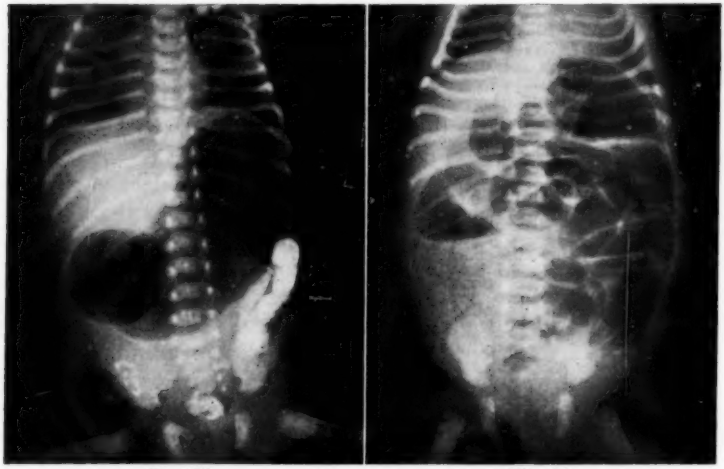

Fig. 28. Fig. 29.

Fig. 28. Flat film of abdomen in duodenal obstruction. Note dilated stomach and duodenum in atresia of duodenum.

Fig. 29. Flat film of abdomen in ileal obstruction. Note dilated small bowel loops and absence of gas in colon with atresia of ileum.

anesthesia; (2) the insertion of a polyethylene cut-down for the administration of hydrating fluids, corrective electrolytes and blood or plasma; (3) the prophylactic use of broad-spectrum antibiotics; (4) positioning the baby with his right side down and electric machine suction handy in the event of regurgitation; and (5) the liberal use of a high concentration of oxygen with temperature and humidity control.

The principles of the surgical technique for managing atresias of the small and large intestines have been clearly defined by Ladd and Gross,[9] and by Gross.[3] Surgeons operating upon newborn babies must familiarize themselves with the writings of these authors.

IMPERFORATE ANUS WITH OR WITHOUT FISTULAS

The anomaly of imperforate anus is a common one (1 in 4000 deliveries). Its early recognition is too often overlooked. A routine part of the examination of every newborn should include the insertion of a finger into the mouth to detect a cleft palate and into the rectum to disclose an imperforate anus. How embarrassing to the physician to have the mother ask about the slit in the roof of her baby's mouth at three months of age after difficulties in formula adjustment. Equally embarrassing to the physician and more seriously important to the baby is to have meconium stools and rectal temperatures recorded for one or two or three days only to discern later that there is no rectal opening. Such a common abnormality should be noted in the first few minutes or hours of life. The varieties are indicated in Figure 30.

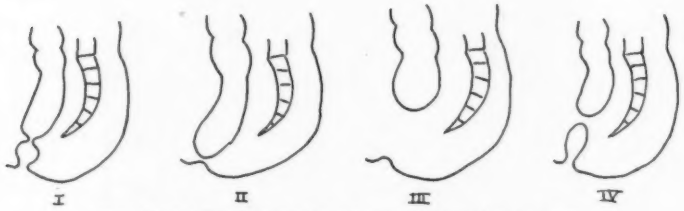

Fig. 30. Schematic drawing of types of imperforate anus.

Once the abnormality is known, definitive treatment is postponed until the baby is twelve to twenty-four hours old. This lapse of time is intentional in order to collect a urine sample to see whether it contains meconium; such a finding means there is a rectovesical or rectourethral fistula which needs special management. In addition, this lapse of time permits ingested air to be propelled through the gastrointestinal tract to the blind rectum. Only after fifteen hours of life have elapsed do upside-down anteroposterior and lateral roentgenograms of the pelvis reveal the length of the imperforation from the rectal gas bubble to the anal dimple (Fig. 31).

In this anomaly early diagnosis is of first significance. For the details of surgical management the reader is referred to the publications of Ladd,[8] Arnheim,[1] and Gross.[3]

OTHER ANOMALIES

The afore-described causes of intestinal obstruction in early infancy are by no means a complete list. We have tried only to emphasize the

most important types with special attention to the necessity for early recognition and prompt, judicious surgical intervention.

In the group of duodenal obstructions *annular pancreas* is now being diagnosed with increasing frequency. This is an embryologic deformity wherein the duodenum is obstructed by a napkin-ring malformation of the pancreas extrinsically compressing the second part of the duodenum.

Fig. 31. Upside-down lateral roentgenogram of infant with imperforate anus. Note that the thermometer in the anal dimple plus contrasting gas in the blind rectal pouch indicates the extent of imperforation.

The clinical picture is similar to and the surgical management is the same as that of atresia of the duodenum. Its recognition is at the operating table, not before.

In the midileum we occasionally see *malrotation with midgut volvulus*. The picture is identical to that of atresia of the ileum except that meconium may be passed normally in the neonatal period. The embryologic abnormality is too complex to describe here, but the reader is referred to the papers by McIntosh,[11] Ladd,[7] Keith[5] and Gross[3] for details.

In the terminal ileum intestinal obstruction in early infancy may be due to *meconium ileus*. Here again the reader will profit by perusing

the papers of Farber,[2] Potts[12] and Gross.[3] Although meconium ileus may be the result of a basic glandular disease with systemic mucoviscidosis, its increasing significance is attributable to its now recognized genetic role as a recessive characteristic in 25 per cent of the American population. More will be heard of this disease with time.

In the colon much attention has been given, in the past few years, to *megacolon*. Swenson[14] has refocused our interest on this long-known disease of older children. Only now are we beginning to recognize its role as a cause of intestinal obstruction in early infancy.

CONCLUSIONS

1. The causes of intestinal obstruction in early infancy are many and varied. They are not due to cancer or degenerative disease, but are primarily architectural deformities. A diagnostic and therapeutic victory does not pay dividends in terms of five-year survivals, but in young citizens restored to normality.

2. Although our mortality and morbidity percentages are today much better than they were yesteryear, there remains considerable room for improvement. General practitioners, obstetricians, pediatricians, radiologists and surgeons can well afford to keep such causes of intestinal obstruction in neonatal life freshly in mind.

3. Earlier recognition and prompt appropriate surgical correction are the cornerstones of improved successes. Early recognition and sound management are emphasized in an elaboration of a few of these anomalies.

REFERENCES

1. Arnheim, E. E.: Congenital Malformations of the Rectum and Anus. Am. J. Surg., *81*:538, 1951.
2. Farber, S.: The Relation of Pancreatic Achylia to Meconium Ileus. J. Pediat., *24*:387, 1944.
3. Gross, R. E.: The Surgery of Infancy and Childhood. Philadelphia, W. B. Saunders Company, 1953.
4. Haight, C.: Congenital Atresia of the Esophagus with Tracheo-esophageal Fistula: Reconstruction of Esophageal Continuity by Primary Anastomosis. Ann. Surg., *120*:623, 1944.
5. Keith, A.: Human Embryology and Morphology. 5th ed. Baltimore, William Wood and Co., 1933.
6. Ladd, W. E.: The Surgical Treatment of Esophageal Atresia with Tracheo-esophageal Fistula. New England J. Med., *230*:625, 1944.
7. Ladd, W. E.: Congenital Obstruction of the Small Intestine. J.A.M.A., *101*: 1453, 1933.
8. Ladd, W. E., and Gross, R. E.: Congenital Malformations of Anus and Rectum. Am. J. Surg., *23*:167, 1934.
9. Ladd, W. E., and Gross, R. E.: Abdominal Surgery in Infancy and Childhood. Philadelphia, W. B. Saunders Company, 1941.

10. Leven, N. L., Varco, R. L., Lannin, B. G., and Tongen, L. A.: Surgical Management of Congenital Atresia of the Esophagus and Tracheo-esophageal Fistula. Ann. Surg., 136:701, 1952.
11. McIntosh, R., and Donovan, E. J.: Disturbances of Rotation of the Intestinal Tract; Clinical Picture Based on Observations in Twenty Cases. Am. J. Dis. Child., 57:116, 1939.
12. Potts, W. J.: Congenital Atresia of the Intestines and Colon. Surg., Gynec. & Obst., 85:14, 1947.
13. Swenson, O.: End-to-End Anastomosis of the Esophagus for Esophageal Atresia. Surgery, 22:324, 1947.
14. Swenson, O.: A New Treatment for Hirschsprung's Disease. Surgery, 28:371, 1950.
15. Vogt, E. C.: Congenital Esophageal Atresia. Am. J. Roentgenol., 22:463, 1929.
16. Wasch, M. G., and Marck, A.: The Radiographic Appearance of the Gastrointestinal Tract during the First Day of Life. J. Pediat., 32:479, 1948.

Physicians and Surgeons Building
Minneapolis, Minnesota

FOREWORD

JEROME GLASER, M.D.

The importance of allergic disease in infancy and childhood has been emphasized the past few years by the recognition of allergy as a subspecialty in the field of pediatrics, and the consequent establishment of a Sub-Specialty Board of Pediatric Allergy under the jurisdiction of the American Board of Pediatrics. It is significant that, in order to be certified in pediatric allergy, the physician must first be certified as a pediatrician. This is highly proper, since allergy in pediatrics is much more intimately associated with general pediatrics than is allergy in internal medicine associated with general medical practice, for example. This is because many of the problems in pediatric allergy are intimately related to the feeding, environment and prophylactic procedures associated with the care of the very young infant and child.

The particularly significant contribution which the pediatrician has to make is prophylaxis. By the early recognition of allergic manifestations, which may occur at any time after birth, and their proper management, the physician may in many instances be able to make life easier for his patients and their parents. Whether or not the statement I once made to the effect that the internist-allergist will eventually deal only with the end products of neglected opportunities in pediatric allergy will ever become true is highly problematical, but is nevertheless an ideal goal.

The physician who knows that colic is sometimes of allergic origin, that gastrointestinal allergy may cause the typical picture of the celiac syndrome, as well as other varied gastrointestinal disorders, that atopic dermatitis (eczema) is frequently the forerunner of pollinosis and bronchial asthma, that the child who has one cold after another or a constantly obstructed or discharging nose probably has this because of an underlying allergy, is in a much better position to help his patients than the physician who is satisfied to treat these conditions only symptomatically.

The well informed pediatrician will not tell the parents to disregard their child's allergies because they will be "outgrown." He knows that there is no way to determine in advance which child will recover from the allergic affliction spontaneously or which child with eczema or asthma, for example, will be compelled because of this policy of neglect to go through adolescence with the physical suffering and psychic trauma which may be so severe in this age period. There is too much which can now be done for these children for such a policy to be considered acceptable practice. With the remarkable progress of pharmacology and the new developments in physiology, particularly those relating to the hypothalamus-pituitary-adrenal axis, the future never looked brighter for the allergic child than it does at this moment. As is the case in all such advances, the details and practical applications must first be worked out by the interested specialist, the processes simplified, and the most useful passed on to those not specializing in this field.

It is the object of this Symposium, not to present a complete picture of allergic disease in children, but to bring to the attention of those interested in children the latest thinking by well qualified pediatric allergists on some of the more important problems in this field.

300 South Goodman Street
Rochester 7, N.Y.

ESSENTIALS OF PSYCHOSOMATICS IN ALLERGIC CHILDREN

RUTH MORRIS BAKWIN, M.D.

THE ASTHMATIC CHILD

The degree to which psychologic factors influence the frequency and severity of asthmatic episodes in children varies widely. In many instances emotional factors are of no moment and the attacks are satisfactorily controlled by the usual techniques. Under these circumstances it would be academic to be concerned about the psychic components.

When, however, the attacks take place frequently and are difficult to control, then the possibility that emotional factors are active should be considered. Anything which upsets the child or makes him unhappy may be the straw which tips the scale and brings on an asthmatic attack.

Psychologic Factors

Given an allergic child with asthma, psychologic factors may influence the episodes in a number of ways:

1. Any circumstance which makes the child anxious and unhappy may intensify the allergic symptoms. The basis may be an unhappy home, difficulty with school work, i.e., reading disability, restricted activity or friction with schoolmates.

A potent factor upsetting the asthmatic child is the bossy or dominating mother. The mothers of allergic children have been repeatedly described as overauthoritative, directing, bossy. "They are capable and competent, and feel threatened if not master of the situation."

From the Department of Pediatrics, College of Medicine, New York University-Bellevue Medical Center, and the Department of Pediatrics, New York Infirmary, New York City.

This is not a very unusual type of mother and is seen in many other instances. She is a difficult mother for any child to take. Most children attempt to adjust to this personality either by submission and compliance or by open rebellion. If the child is resentful, but afraid to rebel, or if for any other reason he represses his aggressive feelings, he may substitute a physical condition for his pent-up emotional problem. An allergic child may have an asthmatic attack or urticaria; another child might vomit or have diarrhea.

Many allergic children doubtless have mothers whose personalities are not so rigid, and these children can adapt better to their environment. In these instances the psychogenic factors play a less important part or none at all and their consideration is not urgent.

Sibling rivalry, difficulties with teachers, and so forth, need not be elaborated. The mechanism is the same. The child unable to cope with his problem shows physical symptoms.

Although asthma is basically allergic, once the pattern of behavior has been established, an attack may be elicited solely by tension-producing situations. The child, finding himself in a difficult position, rebels. He may show his resentment openly with anger and temper or, if repressed, by having an asthmatic attack.

2. The asthmatic child aware of the agitation produced by his attacks and the worry exhibited by his parents finds in his illness a ready means of getting his own way and of evading responsibilities. The choice may be conscious or subconscious. When he realizes that his parents tend to give in to him rather than provoke an asthmatic attack, he may consciously use this technique. Children frequently threaten their parents with "I'll have an attack if I can't do so and so."

3. The child's emotional tension may be increased by a sense of guilt, believing that he may have caused his asthma by not carrying out his mother's directions, for example, by not wearing his rubbers or by eating something forbidden. By becoming ill he hurts himself, and thus his guilt is relieved.

He may be so surrounded by restrictions that he is repeatedly in conflict with himself. When trying to obey his mother or the doctor, he may be considered a poor sport by his playmates for not entering into their games and activities. Indecision will increase his tension. Such a choice is difficult for the child to make.

If his parents, too, have a feeling that allergy in the family or lack of attention to the physician's directions may be responsible for their child's asthma, this guilt feeling will cause them discomfort and anxiety. Their handling of the child will in all probability be protecting and directing. If carried to an extreme, the child will be adversely affected.

4. The attacks are in themselves frightening, and the fear of an attack may upset the child so that his condition becomes worse. If

the child sees his parents disturbed and worried by his attacks, his own anxiety increases.

Illness affects people in different ways. Asthma which limits the child's activity or choice of food, which is often dramatic and frightening, certainly contributes to emotional tension in the child.

5. The child with asthma is, in many instances, chronically ill and presents the characteristics of children ill with any prolonged disease. The bond between mother and child is strengthened, the mother becoming more overprotective and exerting considerable supervision, the child relying on her judgment and accepting direction and authority. When this is carried to an extreme, the child who can no longer submit, reacts in a way characteristic for him. Emotional tension increases, and physical and psychogenic factors become confused.

Psychologic Approach

As with any sick child, the psychologic approach is important. The physician should not be arbitrary in dealing with the situation. The parent deserves an explanation of the child's condition and instruction as to what attitude should be assumed toward him. Even before specific treatment, effort should be directed toward allaying anxiety of both parent and child. This is the humane attitude and the approach to any child. Most physicians have this ability at their finger tips and use it without conscious effort. As it is no more time consuming than skin testing, and is often more productive of results, it can be recommended to the allergist.

History-Taking

Most parents who bring their child to a physician are eager to pour out their troubles. They should be encouraged to talk. From this the physician learns what is important to the parent and also gains some indication as to what kind of parent he is dealing with. Discretion is necessary in obtaining data about parental attitudes toward the child. "How does the child behave?" is a most rewarding question. A parent who is sincerely satisfied with his child's behavior is unlikely to be a rejecting parent. Also this defines the type of conduct the parent desires. Another useful question is, "Is he a happy or moody child?" This may be followed by, "Did you have a happy childhood or did you have difficulties similar to Johnny's?" Happy children do not have deep-seated emotional problems, and parents, satisfied with their own upbringing, are usually successful with their children. Inquiry as to how the child is disciplined, for what, and what the child's reaction is, gives much information.

Play interests and playmates are worth investigation because of the light thrown on the child's own personality. Something can be learned of his adjustment to the limitations imposed by his allergy.

When the child seems well adjusted, the home happy and emotional conflicts minimal, investigation need not be further continued.

Personality

The allergic child in whom a large psychic component influences the symptoms has been described as submissive and immature, irritable, fearful, overanxious and lacking in self-confidence. The need for the parent is excessive. The possibility of separation from the parent or loss of parental approval or even the need to face a situation alone may conceivably be sufficient to produce an asthmatic attack in such a child.

It had been suggested that allergic children are brighter than average, but this seems not to have been substantiated. Little and Cohen[9] have reported, in a study of thirty children with asthma and thirty controls, that the asthmatic children and their mothers set higher goals for themselves than do healthy children, and that these are considerably beyond the level of their actual performance. The significance of this is not clear, but a high level of aspiration has been shown to correlate with feelings of insecurity. Overconscientiousness, the need to do things better than average and striving for recognition and prestige have been mentioned as characteristic of the allergic adult.

Miller and Baruch[11, 12, 13] have attempted a controlled study of rejection. Of 100 allergic children in their series, they found 97 per cent were rejected by their mothers, while of sixty nonallergic children 36.7 per cent were rejected. The difference in the number of rejecting mothers of allergic and nonallergic children was statistically significant, but one must assume a tentative attitude toward the interpretation of what constitutes rejection and the technique used for eliciting this information. Miller and Baruch go on to relate the rejection to the mother's emotional immaturity and poor sexual adjustment. The importance of this and the significance for the allergic child are less easy for the physician to understand, and may in some cases complicate the picture. The recent literature abounds with papers citing the frequency of rejection among the parents (usually the mothers) of asthmatic children.

Rorschach and thematic apperception tests (TAT) have been given to a small number of patients with allergy. These showed that the prevalent character traits were fear, deep-seated anxiety, demanding behavior, striving for recognition, insecurity and passive dependence.

Unfortunately, detailed reports are not presented in most of the papers.

Schatia[15] studied the Rorschach records of forty asthmatics and compared them with clinical impressions. She concluded that there was a fairly definite personality type, largely compulsive. Almost two thirds of the patients showed signs of neurosis. The author cautions against too rigid conclusions until there is confirmation on a larger series.

Although most of these series are small, without adequate controls, and interpretive rather than objective, some effort is being made by psychiatrists to base their opinions on tests rather than purely interview. Most of the studies give a fairly definite and consistent picture characteristic of the allergic person, but probably applying only to the allergic patient in whom emotional conflict is dominant.

Physical Factors

It has been suggested that the behavior disturbances of some children with asthma may be accounted for by local edema within the cranial cavity. The resulting increased pressure may cause headache, vomiting and dizziness. The child with asthma becomes irritable and disagreeable during a seizure. When the offending agent is removed, the child's mental attitude returns to normal. Dees[1] observed electroencephalographic changes in a high percentage of allergic children irrespective of the presence of behavior problems. The abnormality was predominantly occipital dysrhythmia.

Doust and Leigh,[3] with twenty-five asthmatic patients, in whom they measured arterial blood oxygen saturation levels during the course of psychiatric interviews, concluded that "stimuli arising both from within and without the organism, which disturb hemostasis, in persons of a certain constitution and heredity, may produce asthmatic attacks."

These explanations of the physical condition influencing the mental state are hardly more satisfactory than the psychiatrist's view that the emotional attitude is the dominant factor.

Management

That the allergic manifestations and the emotional environment are cause and effect, either one being primary, is not essential to the understanding of the psychodynamics of allergy. Rather the child as a whole, his personality and home, his illness, his own and his parents' reaction to it and the attempt, not only to rid the child of his symptoms, but to provide a milieu in which he can grow normally and thrive, should be the aim of the physician. With some children the psychogenic fact-

tors will be minimal and need not concern the physician; with others they may lead to the continuance of symptoms in spite of adequate therapy.

An important factor in the prevention of emotional problems is an appreciation by the physician of the possibility of their occurence. With an intelligent mother a discussion of her attitude, of which she is often unconscious, may help a great deal. Explaining that each child needs repeated assurance of his parents' affection may appeal even to the rejecting mother. Emphasis may be placed on the importance of the child's developing his own potentialities. His capabilities may be pointed out and his successes applauded. An understanding attitude taken by the physician will help to relieve the tension between mother and child, with decrease in the frequency of emotional conflict and asthmatic attacks.

Arranging a realistic schedule for the allergic child is important. A wise physician will see that sometimes a compromise is necessary. To be like one's companions and to "belong" play a large part in the successful emotional adjustment of a child. If a reading disability or a school difficulty exists, it should be corrected, since any extra problem will make the child unhappy and increase the tension.

Encouraging the child to express his feelings freely, whether they relate to dislike of injections, annoyance at dietary restrictions, jealousy toward siblings or resentment toward his parents, may bring gratifying results. Relief of pent-up emotions is always helpful, and, in addition, valuable information about the child may be gained, and a revision of his schedule to better suit his needs will be possible. If the parent can see the value of this "ventilation," he may be more accepting of the child's expressing his doubts and troubles at home.

The physician should avoid a critical attitude toward the parent and child. One may point out errors in child rearing, make suggestions and lead the parents to discover for themselves better techniques, but the task of attempting the correction of personality distortions in the parent or child should be left to the psychiatrist.

In psychosomatic disorders it is usually best for the physician to continue his contact with the patient and not "turn him over" to a psychiatrist. The parent of the asthmatic child needs help in accepting the psychiatric referral. Also the psychiatrist will be unable to cope with exacerbations of the allergic condition when the child needs prompt and specific medical treatment.

Need for the Psychiatrist

When the anxiety, dependence and rejection are overwhelming, the family needs re-education and reorganization. This is true in allergic

as well as other children, and equally true whether the asthmatic attacks are controlled by medical treatment or persist.

To spend one year, not to say three or four, as detailed by some psychiatrists, in an attempt to cure asthma seems extravagant and expensive. But if the prolonged treatment is necessary to relieve an abnormal emotional situation and the family comes out of the treatment as a healthy integrated unit, the value cannot be doubted.

OTHER ALLERGIC CONDITIONS

Difficult to interpret are the many studies of allergic patients in whom physical changes take place through suggestion or under hypnosis. Cases are recorded of adults having severe attacks of *hay fever* in the presence of artificial flowers or even through the suggestion that flowers or other offending agents were present.

Swelling of the nasal mucosa, hyperemia and other symptoms similar to hay fever coryza have occurred in susceptible patients during interviews in which the patient became anxious, hostile, frustrated and resentful. Through manipulation of the interviews the patient's attitude could be turned on and off with resulting changes in the nasal mucous membranes.

Herpes simplex has been induced through hypnotic suggestion by recalling an unpleasant emotional experience with the simultaneous suggestion of itching. Kepecs and Robin[7] have shown that the rate of exudation, or weeping, of the skin in hypnotized patients with *atopic eczema* and *urticaria* increases under emotional strain and decreases when, through suggestion, the tension is relaxed. They believe that the feeling of tension, unrelated to skin sensations, can cause the patient to scratch. This in turn irritates the skin, causing itching and more scratching.

Food to which one is allergic is usually avoided or, when taken, may cause nausea and vomiting. It has been suggested that food may become associated symbolically with diverse emotional meaning early in life, and that food with unpleasant associations may be avoided or, if eaten, result in disturbing reactions in the gastrointestional tract. Primary *allergenic food reactions* are then followed by secondary psychogenic reactions which may be more incapacitating.

THE AIM OF TREATMENT

There is no dividing line between the physical and emotional components. In all probability both factors should be appreciated and handled. As the allergist is the doctor to whom the child comes for treatment, he would appear to be the logical person to assume the

responsibility. If he will take the time to get a good history, observe the parent and child in his office, and encourage them to discuss their difficulties, he can readily detect emotional tension if such exists.

For optimal development children need support, security and strong acceptance. This holds true for all children, and should be the aim of the physician in his advice to parents. Attention to the emotional and situational problems of the child with allergy in no way precludes other forms of therapy.

REFERENCES

1. Dees, S. C.: Inter-relationships of Allergic and Psychiatric Factors in Allergic Children, in Sociological Foundation of the Psychiatric Disorders of Childhood. Proc. 12th Inst. of the Child Research Clinic of the Woods School, 1945.
2. Dees, S. C., and Lowenbach, H.: The Electroencephalograms of Allergic Children. Ann. Allergy, *6*:99, 1948.
3. Doust, J. W. L., and Leigh, D.: Studies on the Physiology of Awareness: The Inter-relationships of Emotions, Life Situations, and Anoxemia in Patients with Bronchial Asthma. Psychosom. Med., *15*:292, 1953.
4. Holmes, T. H., Treuting, T. F., and Wolff, H. G.: Life Situations, Emotions and Nasal Disease: Evidence on Summative Effects Exhibited in Patients with "Hay Fever." Psychosom. Med., *13*:71, 1951.
5. Kaufman, W.: Some Psychological Aspects of the Treatment of Patients Who Have Food Allergies. Ann. Allergy, *9*:660, 1951.
6. Kepecs, J. G.: Some Patterns of Somatic Displacement. Psychosom. Med., *15*: 425, 1953.
7. Kepecs, J. G., and Robin, M.: Life Situations, Emotions and Atopic Dermatitis. A. Research Nerv. & Ment. Dis., Proc. (1949), *29*:1010, 1950.
8. Leigh, D.: Asthma and the Psychiatrist. A Critical Review. Int. Archives of Allergy and Applied Immunology, *4*:227, 1953.
9. Little, S. W., and Cohen, L. D.: Goal Setting Behavior of Asthmatic Children and Their Mothers for Them. J. Personality, *19*:376, 1951.
10. Mansmann, J. A.: Projective Psychological Test Applied to the Study of Bronchial Asthma. Ann. Allergy, *10*:583, 1952.
11. Miller, H., and Baruch, D. W.: Psychosomatic Studies of Children with Allergic Manifestations. I. Maternal Rejection: A Study of Sixty-Three Cases. Psychosom. Med., *10*:275, 1948.
12. Miller, H., and Baruch, D. W.: A Study of Hostility in Allergic Children. Am. J. Orthopsychiat., *20*:506, 1950.
13. Miller, H., and Baruch, D. W.: Marital Adjustments in the Parents of Allergic Children. Ann. Allergy, *8*:754, 1950.
14. Mitchell, J. H., and Curran, C. A.: A Method of Approach to Psychosomatic Problems in Allergy. West Virginia Med. J., *42*:271, 1946.
15. Schatia, V.: The Incidence of Neurosis in Cases of Bronchial Asthma. Psychosom. Med., *3*:157, 1941.
16. Treuting, T. F., and Ripley, H. S.: Life Situations, Emotions and Bronchial Asthma. J. Nerv. & Ment. Dis., *108*:380, 1948.
17. Watts, M. S. M., and Wilbur, D. F.: Clinical Management of "Functional" Disorders, The Diagnostic Interview. J.A.M.A., *148*:704, 1952.
18. Wolf, S., Holmes, T. H., Treuting, T. F., Goodell, H., and Wolff, H. G.: An Experimental Approach to Psychosomatic Phenomena in Rhinitis and Asthma. J. Allergy, *21*:1, 1950.

132 East 71st Street
New York 21, N.Y.

SKIN TESTS AND THEIR VALUE IN PEDIATRIC ALLERGY

A. MATHESON, M.D.

It may be of interest to briefly review the history of skin testing. Credit must be given to Blackley[1] of England for using the skin test as a diagnostic procedure in pollinosis. His work was remarkably scientific, but little attention was given to it for a long time. Though many persons repeated and verified Blackley's work, it was not until von Pirquet popularized the skin test for tuberculosis in 1907 that attention was focused on the skin test as a diagnostic aid in allergic diseases. Smith[19] in 1909 and Schmidt[17] in 1910 used the scratch technique in diagnosing food allergy. However, it was Schloss[14] in 1912 who, after much experimentation, systematized the scratch technique as an aid in the diagnosis of this condition. In 1914 Goodale[6] advocated systematic use of the scratch test for diagnosing hay fever, and Cooke[3] about the same time, encouraged by the work of Schick on the intradermal test with diphtheria toxin, published his work on the intradermal test in the diagnosis of allergic disease. Then followed the controversy on the relative merits of the scratch versus the intradermal test, which remains to the present day. The next important step was made by Fritz Talbot in 1916,[20] who, instead of using crude substances for testing, began the application of pure proteins of foods and epidermals.

Since that time, skin tests have been popularized by physicians in diagnosing allergic disease. Publicity has aided in a misconception, however, of their value in diagnosis, not only among some professionals, but particularly among lay people.

From the Department of Pediatrics, Sarah Morris Hospital for Children of the Michael Reese Hospital, Chicago.

DIAGNOSTIC VALUE OF SKIN TESTS

There is little doubt that skin testing is an aid in the diagnosis of allergic disease, but, like some other laboratory procedures, it must be properly interpreted and evaluated. One should never resort to skin testing as a routine procedure before careful history and physical examination. Whenever possible, such tests must be interpreted in the light of the clinical picture, introduction and elimination of offenders and their subsequent effect on such clinical symptoms. Only too often I have been presented with reports from skin testing laboratories of numerous positive skin tests to foods as a result of which many foods were omitted from the diet with harmful results on the growth and development of children. Closer study invariably revealed that those positive skin tests to the foods had nothing whatsoever to do with the etiology of the presenting complaint. In many instances these tests were not positive when repeated. It is unfortunate that laymen have been educated to the belief that skin tests are in themselves diagnostic, and so, in many instances, employ technicians to perform these tests before taking the child to a competent physician.

On the other hand, there has been a tendency among certain physicians in the past several years to belittle the value of skin tests in general and particularly to foods. They rely completely on history, elimination diets, intentional feedings and environmental control studies to determine the etiologic allergen for the complaint. No one can deny the value of these procedures, each of which has its limitations, particularly when applied to children; but, in a similar vein, one should not neglect skin testing, which is not only a helpful but also a comparatively simple procedure. Such tests will frequently give a clue to the type of sensitivity present and in many instances indicate the offending allergen. One may be impressed from the history that inhalant sensitivity is present, but it is difficult, in many instances, to determine which inhalant is the offender unless skin testing is resorted to. Similarly, one may be convinced that food allergy is present, but the food least suspected may be the offender.

To illustrate this, may I relate the story, often told by one of America's well known allergists, of a prominent physician who for years thought he was allergic to dates, but ate them because he was extremely fond of them. He later learned that dates were not the offender, but that the vegetable oil used in polishing the dates was the offending allergen.

With our complicated diet, and the many prepared food mixtures on the market, it becomes increasingly difficult to suspect which of the many potential allergens these mixtures contain may be the offending one. One need only recall the several possible allergens in some prepared cereal or vegetable mixtures sold under various trade names, to

realize the complexity of the problem. The following case represents a specific instance when the history obtained was unreliable and when skin testing gave the first indication of the offending allergen.

CASE I. A 3 year old child was brought to the office recently because of a generalized dermatitis of 3 to 4 months' duration. There was a history of eczema in early infancy which was greatly relieved by omission of eggs from the diet and by the use of soybean milk. The mother was convinced that the present skin disease was caused by cow's milk and eggs. "The skin looks exactly as before," she related. This time, however, there was no improvement in the eczema when cow's milk and eggs were omitted from the diet for 10 days. Skin testing (scratch) revealed a 4 plus reaction to horse dander and to rabbit hair. The mother *then* related that for the previous 4 months she had been living with in-laws on a farm where horses were kept and rabbits were raised. On environmental control the skin lesions cleared rapidly, but recurred on another visit to the farm.

GENERAL REMARKS ON SKIN TESTING

The physician is often discouraged with skin testing because of the frequent negative responses with allergens he expects to give positive tests. He may blame the child's skin as being nonreactive, or he may blame the allergen as not being potent. In many instances closer study will reveal that neither is a true explanation. The following case history will illustrate this.

CASE II. A 6 year old child who had gastrointestinal symptoms and dermatitis was suspected to have wheat sensitivity. When skin tests to wheat, both scratch and intradermal, were negative, the physician blamed the child's skin as being nonreactive. He also was ready to discard the testing extract as being nonpotent. That the child's skin was reactive was proved by strongly positive tests with ragweed, dust and Alternaria. That the testing material was potent was proved by a whealing reaction obtained with the same wheat extract on the mother, who presented symptoms of itching of the nose and hands when working with wheat flour.

It is true that in a small percentage of children (approximately 3 to 5 per cent, a slightly higher percentage than in the young adult) the skin is anergic. In general, however, the skin of infants and children is fully capable of demonstrating an antigen-antibody reaction in the form of erythema, with or without whealing, depending on the concentration of antibody present in the skin and the potency of the antigen introduced. Other factors, such as state of nutrition, intactness of circulation, presence or absence of edema, state of morbidity, may also affect the reactivity of the skin. In children an erythematous reaction of the skin is more frequent than whealing. Similarly, multiple sensitivity is frequent. The following remarks may be of aid:

1. All positive tests obtained in a single series of skin tests should be repeated individually to be sure that they are positive. This is particularly true in infants, in whom peripheral lymphatic redistribution in the skin is high, so that a strongly positive test may affect an adjacent questionable positive.

2. The degree of skin sensitivity has little, if any, relation to the

degree of clinical sensitivity. A child may be successfully treated for pollen hay fever to the stage where he is clinically greatly improved, and yet the skin test for pollen may not vary from its original intensity.

TECHNIQUE OF SKIN TESTING

Detailed technique will be omitted here. A Broadbent or a Hill scarifier is satisfactory. The scratch should merely *penetrate* the epidermis, and the tests, when done in a series, should be about 1 inch apart. The sites of choice for tests are the back for infants and young children; for older children the back or lower arms may be used, avoiding proximity to joint areas. In young infants as many as twenty scratch tests can be done at a sitting, and in older children thirty to forty such tests may be done. When positive tests are obtained at a site, it is best to wait several days before that site is used again, because of the tendency of skin in positive areas to remain refractory for several days. For intradermal testing a graduated tuberculin syringe and a 26-gauge ⅜-inch needle are used. Care must be taken that the syringe barrel is tight, in order to avoid air injection, which may produce *wheals*. Not more than 0.02 cc. should be injected for a test. This is just enough to produce a barely visible wheal. Needless to say, all testing should be accompanied by controls. Intradermal testing should be done, preferably on the upper arm so that a tourniquet may be applied if a systemic reaction occurs. The next sites of choice are the lower arm, the back, particularly in infants, and the medial aspect of the thigh.

There is little doubt that intradermal tests are more sensitive than scratch tests. A skin reaction with a 1:50 extract by scratch method can be simulated by an intradermal test of 1:5000 dilution with the same extract. The intradermal test has a few disadvantages, however, the most important being its potential to produce a constitutional reaction. Though such tendency is less in children, yet it is a distinct frightening possibility; some deaths having been recorded from the use of such tests with highly potent material. Another disadvantage of the intradermal test is its greater tendency to produce falsely positive reactions, especially with foods. Unless one has had much experience in testing and a thorough knowledge of the individual allergen potency, it is unwise to resort to intradermal tests without preceding scratch tests. Our own practice is to do scratch tests first and follow the negatives with intradermals of proper dilution, if necessary. Needless to say, it is not only unnecessary but also dangerous to follow a positive scratch test with an intradermal test of the same allergen. It is important to avoid testing with a group of related potent allergens at the same session. Some of the extremely potent materials are fish, nuts, silk, glue, cottonseed, horse dander, pyrethrum, flaxseed, mustard and pollen. There is little if any truth to the opinion often expressed that

cutaneous sensitivity is greatly diminished during or immediately after an asthma attack.

What and How Many Substances to Test For

This is a moot question that to a certain extent will vary with the clinical condition, the history and the geographic locality. It is obviously unnecessary to test children to substances they do not come in contact with. On the other hand, experience tells us that certain foods, inhalants and contactants are common sources of exposure. In a general way too little testing is just as unwise as too much testing and probably more harmful, since it may lead to wrong conclusions. The following is a list of substances which should be available for testing:

Allspice	Corn	Lima bean	Rabbit hair
Almond	Cottonseed	Milk (cow's)	Ragweed
Alternaria	Dates	Mucor	Red top
Apple	Dog hair	Mustard	Rhubarb
Aspergillus	Eggwhite	Navy bean	Rice
Banana	Elm	Oak	Rye
Barley	Flax	Oats	Salmon
Beef	Flaxseed	Onion	Sardine
Beets	Feathers (chicken)	Orange	Sheep wool
Birch	Feathers (mixed)	Orchard grass	Shrimp
Buckwheat	Garlic	Orris root	Silk
Burweed marsh elder	Halibut	Peach	Strawberry
Cabbage	Helminthosporium	Peanut	String bean
Carrot	Hormodendrum	Pear	Timothy
Casein	Horse dander	Penicillium	Tomato
Cat hair	House dust	Perch	Tragacanth
Celery	June grass	Pineapple	Trout
Cherry	Jute	Plantain	Tunafish
Chicken	Kapok	Poppyseed	Wheat
Cocklebur	Karaya gum	Pork	Whitefish
Cocoa	Lambs quarters	Potato	Yeast
Cod	Lettuce	Pyrethrum	

A glance at this list will immediately suggest that, depending on factors previously mentioned, many of these substances may be omitted and others added. It is important to remember that multiple sensitivity is the rule rather than the exception, and that though one allergen may be the major offender, other allergens may also contribute to the child's clinical state of sensitization. Thus, in simple pollen hay fever, though ragweed may be the major offender, dust, fungi and foods may contribute, and better clinical results are obtained by considering these factors.

Scout Testing

There are certain limited situations in which there is a great doubt whether the clinical condition is on an allergic basis and in which,

therefore, extensive testing is not indicated. In these situations one may proceed with a limited list of allergens which in our experience are frequent indicators of atopic hypersensitiveness. When these are negative, one may reasonably feel that it is unnecessary to proceed with further skin testing. Such tests include:

Milk	Hormodendrum	Horse dander	Beef
Wheat	Helminthosporium	Cottonseed	Orris root
Buckwheat	Tree mixture	Kapok	Fish
Eggwhite	Cat hair	Silk	Chocolate
House dust	Dog hair	Peanuts	Pecans
Grass mixture	Feathers	Potato	
Alternaria	Cow hair	Corn	

Indirect or Passive Transfer Testing

This is a method of testing first described by Prausnitz and Küstner in 1921.[11] Its purpose is to demonstrate the presence of a specific antibody in the serum of an allergic person. This antibody can in many instances be transferred to the skin of a nonallergic person and demonstrated on such a normal skin by injection into the site of the corresponding antigen with a resultant immediate type of reaction. It is useful in cases in which direct testing is not possible, as in severe, generalized atopic dermatitis or other generalized skin rashes. It may also be used in cases of chronic eczema of older children, with leathery skin, in cases of dermatographism, chronic urticaria or when there is antipathy on the part of parents to direct skin testing. It is also useful when there is a desire to check the validity of an unusual number of positive skin tests by the direct skin testing method. Its limitation is that it is frequently difficult to obtain potent antiserum, and its usefulness is limited in the great majority of instances to the atopic type of hypersensitiveness. About 5 to 10 per cent of the skin of children as well as adults will fail to react positively to a passive transfer test in known cases of specific sensitivity. In general, however, it is a valuable test and a great step in improving one's diagnostic technique. It can be used as an office procedure.

Testing in the First Year of Life

The statement is often made that it is useless to test young infants, since skin tests on them are frequently negative. Our recent experiments[9] have convinced us that the skin of such infants is easily capable of demonstrating an antigen-antibody reaction in the form of erythema or whealing, depending on the concentration of antibody in the skin and the potency of the atopen used. It is not the age of the infant, but the clinical type of allergic condition under consideration, and the

presence or absence of antibodies in the skin, as well as the potency of the allergenic extract used for the test, that are the determining factors. Thus strongly positive whealing skin reactions to eggwhite are common in very young allergic infants, particularly when eczema is present. Similarly, it is not unusual to obtain positive skin tests to milk and wheat and, after the first several months of life, to various inhalants as well. Why one should expect to get positive tests to dust, feathers, pollens, and the like, in the first few months of life is hard to understand.

Although, theoretically, all that is necessary for development of sensitization is re-exposure after an incubation period, one must realize that the great majority of substances we come in contact with are poor atopens, and it requires repeated or massive exposure in these young infants for sensitization to develop. It is true that in exceptional cases, when the infant has great inherent potential sensitivity or is exposed repeatedly to massive inhalant doses, clinical sensitivity to such inhalants can be acquired early. Such cases will frequently give positive skin tests to inhalants very early in life, but, as previously stated, these instances are not common. In general, it may be stated that infants in the second six months of life will give positive skin tests more often than in the first six months and about twice as often in the second year of life as in the first. It is highly important to use both scratch and intradermal testing techniques in these infants. Many negative scratch tests will give true intradermal positive results.

Table 26 illustrates results of skin tests in the first year of life in a group of infants with eczema.

TABLE 26. *Skin Tests on 37 Infants with Atopic Dermatitis, 4 to 12 Months of Age*

	SCRATCH POSITIVE	ADDITIONAL INTRADERMAL POSITIVE	TOTAL POSITIVE	PERCENTAGE
Milk	4	6	10	27
Eggwhite	16	4	20	54
Wheat	3	5	8	21
Orange	0	3	3	8
House dust	2	4	6	18
Alternaria	0	3	3	8
Fish	0	1	1	3

Skin Testing to Foods

Absorption of unaltered or partially altered protein from the gastrointestinal tract of human beings is a normal physiologic process and has been demonstrated by many investigators, including Schloss,[16] Ratner and Gruehl,[18] and others, as well as by the author.[9] In nonatopic persons such absorption is probably minimal, though temporary

positive skin tests may be obtained. Thus Schloss and Myers,[15] in studying normal newborn infants who were fed cow's milk for the first time, found that, after ten to sixteen days, precipitins for cow's milk appeared in the blood. These precipitins were present in small quantities and disappeared in a short time, though the infants continued to consume cow's milk. DuBois and co-workers,[4] in similar studies on normal newborn infants who were fed cow's milk for the first time, found that, in addition to precipitins, skin-sensitizing antibodies to cow's milk, with production of positive skin tests to the same allergen, were regularly present. These positive skin tests also were temporary and disappeared in a few weeks in spite of continued milk consumption. In atopic children, however, such absorption of foreign protein produces these same antibodies, which not only sensitize the skin with greater regularity and persistence, but also may sensitize certain other shock organs with production of symptoms of varying degree, depending on the state of susceptibility as well as degree and frequency of exposure. In general, a positive skin test to a food indicates past, present or potential sensitization to that food. In the infant or very young child such positive tests, especially scratch tests, are more likely to signify clinical sensitization than in the older child or adult. This interpretation is not applicable to the frequently positive tests to eggwhite in young infants, especially when eczema is present. In the majority of these instances the positive test to eggwhite merely indicates basic congenital sensitization. Even in these instances, though egg may not be the primary etiologic allergen, it is frequently a contributing factor in the clinical complaint.

In older children the association of positive skin test to foods, with clinical symptomatology, has the same status as in adults. In many instances (approximately 50 per cent) such positive skin tests merely indicate past or nonspecific sensitization and are not responsible for clinical complaints. Negative skin tests to foods do not by any means rule out their clinical significance. Thus, such violent allergens as fish and nuts, which frequently cause symptoms, are, according to Leibowitz,[8] far down the list in production of positive skin tests. The same is true for milk, wheat and chocolate. On the other hand, such foods as lettuce, tomatoes and spinach frequently produce positive skin tests, but seldom are responsible for allergic symptoms. For these reasons there is much controversy as to the value of skin testing to foods in the older child or adult, and Randolph[12] and others have completely relied on history, elimination diets and intentional feeding as diagnostic methods. Hill[7] found correlation between skin tests to foods and respiratory allergy in only about 20 per cent of asthmatic children.

In the final analysis a positive skin test to food in the young infant is of much greater clinical significance than in the older child or adult.

In our experience, foods are more likely to play a significant role in atopic dermatitis, urticaria and gastrointestinal disturbances than in respiratory allergy. In all cases, whenever possible, the evaluation of results to skin tests with foods should be correlated with history, results of elimination diets or intentional feeding. One must remember that in some instances multiplicity of positive skin tests to foods can be attributed to antigenic relationships between various allergens. For instance, there is such relationship between chicken feathers, hen's eggs and chicken meat; similarly there is such relation between milk and beef; and celery, parsnips and carrots.

Skin Tests to Inhalants and Pollen

Positive skin tests to inhalants are of greater clinical significance than positive tests to foods. Such positive reactions are frequent after the first six to twelve months of life, though occasionally sooner. The inhalants include dog hair, cat hair, feathers, house dust, kapok, mohair, rabbit hair, horse dander, flaxseed, molds, pollens and others, depending on the locality.

It should be remembered that extracts of house dust, feathers and dog hair frequently act as skin irritants because of difficulty in purifying such extracts, and one must be careful in evaluating their significance unless immediate whealing reactions are obtained with them. A word of warning on intradermal testing with Endo's house dust may be of value. This preparation is a powerful allergen; if an intradermal test is indicated, it should be done with a highly diluted extract, 1:20,000 or 1:40,000. Inhalants are the most frequent etiologic agents in respiratory allergy. They are also important in atopic dermatitis of older infants or children. For this reason thorough skin testing with these substances is a highly valuable procedure. It is also important for the physician to acquaint himself thoroughly with the environmental sources of these inhalants.

Skin testing in respiratory pollinosis, particularly hay fever, is extremely important. In this situation greater correlation occurs between positive skin tests and clinical symptoms. Such correlation is more frequent in pollen hay fever than in pollen asthma. In young children the classic symptoms of hay fever are frequently absent, and symptoms may be mild, so that many cases are diagnosed as "summer colds." Seasonal asthma should always lead to a suspicion of pollinosis as the etiologic factor. In early hay fever negative scratch tests to pollen should always be followed by intradermal tests.

There are certain other factors to remember in skin testing with pollen. It is not too uncommon to have a negative skin test to pollen in the presence of pollen asthma, with or without pollen hay fever, and in

such cases the inhalation of pollen or the conjunctival test with pollen may produce positive symptoms. Similarly, in early pollinosis dermal sensitivity may not be fixed, and one may obtain a negative test before the season and a positive test only during the pollen season. It may require a few seasons before the dermal sensitivity is fixed, particularly with ragweed. With grass pollen, on the other hand, dermal sensitivity often precedes mucous membrane sensitivity and clinical symptoms. Ragweed-sensitive patients will often have a positive skin test to goldenrod (which is an insect-borne pollen), burweed marsh elder, cocklebur or pyrethrum. The latter four allergens have a botanical relationship to ragweed. Most of the inhalant allergy caused by tree pollen in early spring is, in our locality, attributed to the hardwoods. Though such trees pollinate abundantly, sensitivity to these pollens in children is usually mild except in parks, forests or other heavily wooded areas.

DO SKIN TESTS CHANGE?

It is common knowledge among allergists that positive skin tests to inhalants and pollen seldom become negative, whereas positive tests to foods may readily become negative if contact with these foods is avoided for a variable period. Positive skin tests to such foods in infants or young children frequently become negative before the age of seven years and sometimes sooner. The exception to this is skin sensitivity to such violent allergens as fish and nuts. The skin sensitivity to inhalants such as animal dander, house dust, pollen or others practically never disappears regardless of avoidance of contact or hyposensitization. It becomes evident, therefore, that a case of pollen hay fever may be treated successfully and still remain with a positive skin test. I reiterate that this need not apply to early acquisition of pollen sensitivity, when the skin test may vary from negative to positive and back to negative until dermal sensitivity becomes fixed. Certain drugs such as epinephrine or the antihistaminics, if taken before skin testing is to be done, may interfere with tests and change slight positives to negatives. ACTH or cortisone has little or no effect on the immediate skin reaction. It is highly important in children to retest periodically, since children will acquire new sensitizations.

The thirty-seven infants with atopic dermatitis, the results of whose skin tests are shown in Table 26, were retested in later childhood and adolescence when they presented other major allergic manifestations such as hay fever and asthma. The results of these later tests are shown in Table 27.

It can be seen from Tables 26 and 27 that many of the children and adolescents lost their skin sensitivity to some foods and acquired greater skin sensitivity to inhalants and pollen. It is also interesting to know that in the majority of cases, which included allergic rhinitis, pollen

hay fever and bronchial asthma, the positive skin tests to the inhalants were of etiologic significance.

TABLE 27. *Skin Retesting in Later Childhood and Adolescence, 7 to 16 Years of Age*

	SCRATCH POSITIVE	ADDITIONAL INTRADERMAL POSITIVE	TOTAL POSITIVE	PERCENTAGE
Milk	2	3	5	13
Eggwhite	6	2	8	21
Wheat	2	2	4	10
Orange	0	0	0	0
House dust	6	14	20	54
Alternaria	3	9	12	32
Fish	3	2	5	13
Ragweed pollen	9	6	15	40

DELAYED REACTIONS

Delayed reactions to skin tests occur twenty-four to seventy-two hours after the test has been performed. These are much more common after the intradermal than the scratch test and closely resemble the tuberculin type of sensitivity. They are more frequently noted on testing with foods and bacterial extracts. Their clinical significance is not at all clear, though it is safe to say that in testing with bacteria they are of no clinical significance in the great majority of cases. Whether they signify an early sensitization or low grade sensitization in the case of foods, as a result of modifying the allergen by cooking or by gastric digestion, is debatable. Vaughan[21] believed that when a delayed reaction occurs after a scratch test with a food, in the absence of an immediate reaction to the same, it may represent allergenicity.

THE PATCH TEST

The patch test is used as a diagnostic aid in contact dermatitis. It does not apply to the atopic type of hypersensitiveness. Commercial, ready-made patch test covers are readily available. These contain a center disk on which the suspected contactant is placed, and the cover is applied to the back, upper arm or, preferably, to an area not too distant from the local lesion on the skin. A positive test produces erythema, edema and frequently vesiculation at the applied site within twenty-four to seventy-two hours. Commercial oleoresin extracts of plants or special extracts in case of suspected food dermatitis are also readily available. This test has its limitations, since the particular testing substance may be a potent sensitizer and, if often repeated, may sensitize a previously nonsensitive child. It is also possible that the existing sensitization may

be localized to the area of contact with the substance, and on such an occasion a negative result will be obtained if the test is performed distant from the lesion on the skin. On the other hand, if the test is applied too close to the area of dermatitis, a marked aggravation of the existing lesion may result. It is well to remember that, though such a positive test usually indicates clinical sensitivity, it may, in some instances, merely denote past or potential sensitization. Generally, unless one suspects a certain specific contactant or a group of contactants as the sensitizer, this test is of limited practical value in children.

SKIN TESTING FOR PENICILLIN SENSITIVITY

With continued widespread use of penicillin, the problem of sensitization with the possibility of pencillin anaphylactic-like reactions has become a distinct hazard in penicillin therapy. Since Waldbott's[22] report of death in an adult following intramuscular injection of crystalline penicillin G in 1949, there have been additional reports of such deaths by Mosko,[10] Siegal,[18] Christenson[2] and others. These authors also presented many cases of anaphylactic-like reactions to penicillin with recovery. Though I have been unable to find recorded deaths in children from penicillin administration, I know of two unrecorded deaths. It is interesting to note that in the great majority of instances of penicillin anaphylactic reactions the skin test to penicillin has been uniformly positive.

To gain some idea of the value of the skin test to determine penicillin sensitization in children who had previously had penicillin therapy, we proceeded with skin testing experiments. For the scratch test one drop of aqueous penicillin G was used in a concentration of 5000 to 25,000 units of penicillin per cubic centimeter. For the intradermal test, 0.02 to 0.05 cc. of a solution containing 1000 units of penicillin was used. (Weaker solutions were used when there was history of previous clinical symptoms following penicillin administration.) Briefly, our results were as follows:

1. Not a single positive skin test to penicillin was obtained in 200 children who had previously received many courses of intramuscular penicillin injections. Approximately 6 per cent of the group gave a history of vague symptoms following previous penicillin injections. These symptoms were of delayed variety and in most instances were in the form of either skin rashes or urticaria.

2. From a group of sixty children in the Allergy Clinic, a large percentage of whom had had courses of penicillin injections, no positive skin tests to penicillin were obtained.

3. Skin tests with penicillin on five children who had immediate anaphylactic-like reaction to penicillin administered intramuscularly and three of whom were hospitalized for this, were positive. In four of these

five cases we obtained positive passive transfer tests with penicillin as well. Three of these children gave a history of previous bronchial asthma episodes.

Significance of Skin Tests with Penicillin

1. The great majority of children who have had numerous courses of penicillin therapy do not demonstrate skin hypersensitivity to penicillin.
2. A negative skin test with penicillin in children who have had previous administration of penicillin does not rule out the presence of clinical penicillin hypersensitivity.
3. Although a positive skin test does not signify a clinical allergic reaction to subsequent penicillin administration, it does indicate penicillin hypersensitivity.
4. A positive skin test to penicillin combined with a history of clinical symptoms of some type to previous penicillin administration is strongly suggestive of clinical penicillin allergy. When, in addition, there is a history of atopic allergy—particularly asthma—in the child, a strong possibility of a serious anaphylactic-like reaction to subsequent penicillin administration exists.
5. There is apparently no relation between penicillin and *Penicillium* skin hypersensitivity.

SUMMARY

1. A brief history of the evolution of skin testing in allergic disease is presented. It is pointed out that such a test, similar to other laboratory procedures, is helpful in the diagnosis of allergic disease.
2. Experience and specific knowledge are required in the interpretation and evaluation of the results of skin testing.
3. One who uses the skin test as a short cut in seeking the etiologic agent for a complaint based on allergy will be greatly disappointed as well as misled.
4. Essentially the skin test is based on an immunologic mechanism and results from an antigen-antibody reaction.
5. The various techniques of skin testing are presented, stressing interpretive difference of results as applied to infants and children.
6. The skin of children and even infants is capable of demonstrating an antigen-antibody reaction. Such reaction may be in the form of erythema or whealing.
7. The passive transfer test is a valuable method of skin testing those children whose skin is not fit for direct testing. It is also useful for checking the validity of an unusual number of positive skin tests obtained by direct skin testing.
8. The comparative interpretative value of skin tests to foods and

inhalants is discussed. Positive skin tests to foods in the infant or very young child are frequently of clinical significance. In the older child such positive tests to foods must be checked with other procedures before their clinical significance can be proved. Negative skin tests do not rule out the particular allergen as being clinically etiologic.

9. The significance of the skin test for determination of penicillin sensitivity is discussed.

10. Proper education of the layman as to the value of skin tests in allergic disease is highly advisable.

REFERENCES

1. Blackley: Experimental Researches on Causes and Nature of Catarrhal Aestivus. London, Tindall & Cox, 1873.
2. Christenson, W. N., Hedrick, G. W., and Schugman, R. F.: Fatal Anaphylactic Reaction Following Penicillin Injection. U.S. Armed Forces M. J., *4*:249, 1953.
3. Clarke, W. T.: Beginnings of Allergy. Ann. Allergy, 378:83, 1948.
4. Cooke, R. A.: Treatment of Hay Fever by Active Immunization. Laryngoscope, *25*:108, 1915.
5. DuBois, R. O., Schloss, O. M., and Anderson, A. E.: The Development of Cutaneous Hypersensitivity Following Intestinal Absorption of Antigenic Protein. Proc. Soc. Exper. Biol. & Med., *23*:176, 1925.
6. Goodale, J. L.: On the Anaphylactic Skin Reactions Excited in Hay Fever Subjects by the Pollen of Various Species of Plants. Boston M. & S. J., *171*:695, 1914.
7. Hill, L. W.: Food Sensitivity in Asthmatic Children. New England J. Med., *238*:657, 1948.
8. Leibowitz, H., Chester, A., and Markow, H.: Foods, Skin Testing and Intentional Feeding. J.A.M.A., *144*:993, 1950.
9. Matheson, A., Greengard, J., and Nierenberg, M.: Reactivity of the Skin of the Newborn Infant. Pediatrics, *10*:2, 181, 197, 1952.
10. Mayer, P. S., and others: Penicillin Anaphylaxis. J.A.M.A., *151*:351, 1953.
11. Prausnitz, C., and Küstner, H. H.: Studien über die Ueberempfidlichkeiten. Centralbl. f. Bakt., *86*:160, 1921.
12. Randolph, T.: Management of Food Allergy. M. Clin. North America, 32:245, 1948.
13. Ratner, B., and Gruehl, H. C.: Passage of Native Proteins through Normal Gastrointestinal Wall. J. Clin. Investigation, *13*:517, 1934.
14. Schloss, O. M.: A Case of Allergy to Common Foods. Am. J. Dis. Child., 3:341, 1912.
15. Schloss, O. M., and Myers, C.: Intestinal Absorption of Antigenic Protein. Proc. Soc. Exper. Biol. & Med., *23*:180, 1925.
16. Schloss, O. M., Anderson, A. F., and Myers, C.: Intestinal Absorption of Antigenic Protein by Normal Infants. Proc. Soc. Exper. Biol. & Med., 23:180, 1925.
17. Schmidt, H.: Beiträge zum Studien der cutänen Allergien. Arch. F. Kinderh., *53*:349, 1910.
18. Siegal, S., Steinhardt, R. W., and Gerber, R.: Fatal and Near-Fatal Penicillin Anaphylaxis. J. Allergy, *24*:1, 1953.
19. Smith, H. L.: Buckwheat Poisoning, with Report of a Case in a Man. Arch. Int. Med., 3:350, 1909.
20. Talbot, F. B.: Asthma in Children. Boston M. & S. J., *175*:91, 1916.
21. Vaughan, W. T.: Practice of Allergy. St. Louis, C. V. Mosby Company, 1939, p. 183.
22. Waldbott, S. L.: Anaphylaxis and Death Due to Penicillin. J.A.M.A., *139*:526, 1949.

30 North Michigan Avenue
Chicago 2, Ill.

GENERAL MANAGEMENT OF ALLERGIC CHILDREN

BRET RATNER, M.D.

In chronic diseases the physician is often unable to accomplish much rapidly and he is therefore deprived of a certain source of satisfaction. Being frustrated, he tends to withdraw from the situation. He may either treat each episode symptomatically or refer the case to a specialist.

Because allergy is being branded as a psychosomatic disease with the implied emphasis on the psyche, the physician is in a dilemma. Should he refer his allergic cases to the psychiatrist or the allergist?

Adequate and comprehensive treatment of the allergic child should involve the following:

1. An approach on an allergic basis, i.e., the extensive and searching investigation through the history, skin testing, elimination of the offending substances and the building up of an adequate state of immunity over a period of years.

2. A complete investigation of the child's constitutional make-up, i.e., diagnosis of a possible hypothyroidism and adequate treatment of it, or diagnosis and treatment of a possible anemia or nutritional deficiency, and so on.

3. Constant diagnosis and treatment of the infectious episodes that occur frequently in respiratory allergy of childhood and tend to simulate true asthmatic attacks.

4. Understanding and treatment of the emotional levels involving both the child and his parents.

The majority of physicians are insufficiently informed about the subject of allergy, particularly in children, and are not cognizant of the

From the Department of Pediatrics, New York Medical College, and Flower and Fifth Avenue Hospitals, New York City.

fact that these diseases can be guarded against and remedied. They assume that for the most part allergy is an inherited condition for which little can be done except to give immediate symptomatic treatment. Many labor under the notion that children usually outgrow their allergies. Though this is true in many instances, the fact that more than 50 per cent of adult sufferers have had their allergy since childhood attests to the fact that allergy is not always a self-limited disease. In the mildest cases allergy is a nuisance. In more severe cases it may be painful and disfiguring. In extreme cases it may keep the child from normal development and incapacitate him for life. Hence it is important to treat allergy in childhood.

The role of heredity in allergy has for many years been tacitly accepted by most students of this subject. However, Ratner and Silberman,[1,2] from data of their own and in a critical review of the subject, do not support this hypothesis. They state: "In view of the conflicting conclusions that have been drawn by different investigators thus far in an attempt to apply mendelian laws to allergy, the difficulty in obtaining adequate material and the inadequate definition of essential criteria, no genetic hypothesis can be made to fit the existing data."

A physician may refer a child whose asthma he feels is psychologically initiated. Yet after the allergist has made a thorough and painstaking investigation, including endocrine and metabolic studies, and, thus guided, has treated the patient, the allergic symptoms will be improved or abated despite the persistence of disturbing psychologic facets.

Asthma will often exist coincidentally with mental illness because of the relatively common occurrence of both. As yet no scientific evidence has been presented as to a dynamic interrelationship between the two disorders.

HISTORY

At the outset, discussion of the chief complaint gives the mother an opportunity to tell the doctor the story as she knows it. Such informal discussion can be fruitfully directed by many searching questions. A good history is essential in the evaluation of an allergic case. As specific episodes are unfolded, one can get an idea of when they occur, what circumstances surround them, the nature of the episodes and many facets which were not adequately covered by the recital of the general complaint.

Clarification is often obtained when the parent is asked to describe the last typical attack, which should be given in great detail. This information gives a good idea of what the child is actually suffering from. For example, if the child has not had eczema, urticaria, gastrointestinal

symptoms or angioedema, and has no history of food intolerance, one can tentatively speculate that foods are not involved.

If there is no history of hay fever, eye symptoms or cough, one may assume that pollen is not a factor. Positive information in either of these categories is provocative evidence for a diagnosis of food allergy on the one hand and pollen allergy on the other.

If one finds that the present symptoms persist throughout the year and are accompanied by respiratory distress, the assumption is that the child has asthma. Further questioning may reveal whether the respiratory symptoms are seasonal, pointing toward a relationship with pollens, or are perennial, thereby incriminating other environmental factors.

If the respiratory symptoms are related to foods, the condition may be accompanied by eczema, urticaria or gastrointestinal symptoms. An antepartum history of food cravings, excessive indulgence in certain foods, the excessive use of drugs, endocrine disturbances or transfusions during pregnancy may all be significant.

The neonatal history may also have some bearing on an analysis of the case by helping to rule out some congenital anomalies.

Questions pertaining to birth weight and general development are important, since they may point to some constitutional deficiency such as hypothyroidism.

The early feeding history of the child may indicate excessive indulgence in certain foods or a bizarre diet. One must continue in the collection of information, time after time, getting data on reactions to foods taken for the first time or even after repeated contacts, and environmental experiences such as visits to certain places.

The history of contagion may reveal repeated attacks of so-called pertussis or pneumonia which in truth were forerunners of allergy. Repeated attacks of so-called measles or other eruptions are often later shown to have been allergic episodes.

Gastrointestinal disturbances have been diagnosed as acute appendicitis, intussusception, pyloric stenosis or celiac disease and later shown to have been due to food allergy.

Particular attention should be paid to the type of drug the patient has been taking, for it may be the cause of a profound allergy.

It is important to go into a detailed inquiry into the child's habits. The question of fatigue, response to studies, intellectual status and kindred minutiae are of importance. Psychologic adjustments must be evaluated.

The following case bears out the importance of a careful history.

CASE HISTORY. A boy of 9 years suffered from much gastrointestinal distress. His difficulty was attributed to a diaphragmatic hernia, which was corrected surgically. Hence it must be assumed that these specific symptoms were not allergic in character. In addition, however, the child was always fatigued and slept a great deal. He showed

many indications of nervous instability and did poorly in his studies. Furthermore, he stammered. We discovered that he was basically left-handed, but had been forced to use his right hand. These constitutional difficulties were coupled with a history of hay fever, vernal catarrh and asthma. Our investigations further indicated that the boy suffered from hypothyroidism. His allergic symptoms were proved to be due to pollens and inhalants.

That some of the boy's difficulties might have been overlooked if so detailed a history had not been taken is obvious.

Composite therapy was instituted, consisting in (1) correction of the diaphragmatic hernia, (2) specific treatment for his allergic hypersentivities, (3) specific treatment for the hypothyroidism, and (4) insistence that he be permitted to use his left hand.

Had not all his difficulties been managed at the same time, it is doubtful whether such good results would have been achieved.

A most detailed history is essential.

PROTEIN SKIN TESTS

Without benefit of the skin tests, I doubt whether the treatment of allergy would have made the strides it has. Skin tests are, however, not the all-encompassing diagnostic tools in allergy. They have guided us by focusing attention on possible etiologic factors.

Through skin testing we are able to state with a fair degree of assurance that one person is sensitive to eggwhite and another to ragweed. Nevertheless the skin test is fallible. At times the skin is insensitive, and there are many other problems involving antibody fixation and chronologic and topical relations. As the child develops, new skin sensitivities may rise which were not present when the child was originally tested. Yet with all its inadequacy and imperfection it is the best test thus far devised and compares favorably with other biologic methods of diagnosis.

There is a tendency at present to do a few selected skin tests suggested by the history. In my estimation this is unwise and unsound. Despite their shortcomings, skin tests are significant when properly evaluated. We perform approximately 400 tests, which include the majority of native pollens, molds, inhalants, bacteria and foods with which the person may come in contact. Often tests are made with material obtained from the direct environment of the patient.

We use both the scratch and intradermal methods of testing. The scratch test is especially valuable in determining the degree of activity; i.e., a positive reaction by scratch test generally indicates that the patient is highly allergic. The intradermal method gives more false reactions than the scratch test. The protein extracts of fruits, vegetables and condiments are notorious for giving a high incidence of false reactions when injected intradermally. On the other hand, with children an excessive number of negative tests are obtained with pollens and inhalants applied by the scratch method.

In summary, the scratch tests are better to determine food sensitivity in childhood, whereas the intradermal method is better for pollens and other inhalants. A positive scratch test as a rule indicates a high degree of sensitivity, whereas a positive intradermal test does not to the same extent.

For a physician to diagnose a true allergy, he must give evidence that the child is sensitive to one or another substance. Herein lies the distinction between the somatic and the psychologic approach.

TREATMENT

In the evaluation of a case, consideration must be given to careful history, physical findings, constitutional factors, endocrine and psychosomatic factors, blood studies, nasal cytologic studies and fluoroscopic and roentgenologic findings, in addition to careful skin testing. Many of these data are not static, but undergo change.

It is the evaluation of all these factors which makes for proper orientation and treatment. In the case of respiratory allergy, for example, one may discover an infectious sinusitis or an allergic or bacterial pneumonitis. A cytologic change in the nasal secretion might point to an allergic or infectious episode. Yet to the casual observer all these episodes would be symptomatologically diagnosed as allergic. Treatment on such a basis would be ineffective. Each incident must be carefully differentiated and treated accordingly.

The same may be said of dermal allergy. One episode may be allergic in origin, another might be due entirely to secondary infection. Likewise a dermal condition may be related to a hypothyroidism or be psychosomatic in origin. It takes years of experience for the trained allergist to analyze and track down each allergic episode, and this cannot always be done.

Many therapeutic measures have been sought. Today we are living in the era of the so-called antihistaminic drugs. Clinical trial has given us some evidence of their accomplishments. They have proved to be effective in the alleviation of symptoms of pruritus, nasal and lachrymal secretions, and edema. But they have failed to give significant relief in asthma or the more serious forms of dermal allergy, both of which are the graver and more frequent manifestations in the field of allergy. From their mode of action it is obvious that these drugs act only as palliative agents. They do not eliminate the basic mechanism responsible for allergic symptoms.

We are not prepared, as yet, to finally evaluate the roles of ACTH and cortisone in allergy. Up to the present they have been shown to be largely palliative agents that do not change the basic course of the disease.

The allergy case must not be treated solely symptomatically. The parents must be educated and taught how to handle minor episodes. Preventive measures must continually be emphasized. Immunologic and psychosomatic treatment, as well as proper general care, builds these children up so that allergic episodes disappear almost entirely, if not entirely, and the general well-being of the child is improved. I know of no disease syndrome in childhood that is so intimately bound up with the status of the individual as a whole.

There are times when the challenge is extremely great and the expected results are not realized. In most instances a failure to achieve good results can be attributed on the one hand to an incomplete diagnosis and on the other to a lack of cooperation by the parents.

It is the study of the many ways and means that antigens have of invading the body and producing interreactions with tissue antibodies which offers the greatest hope for prophylactic and therapeutic results.

REFERENCES

1. Ratner, B., and Silberman, D. E.: Allergy—Its Distribution and the Hereditary Concept. Ann. Allergy, *10*:1, 1952.
2. Ratner, B., and Silberman, D. E.: Critical Analysis of the Hereditary Concept of Allergy. J. Allergy, *24*:371, 1953.

50 East 78th Street
New York 21, N.Y.

COW'S MILK ALLERGY IN INFANTS

NORMAN W. CLEIN, M.D.

Breast milk is not only the best food, but is also the ideal and natural food for the newborn infant. Few infants are allergic to breast milk, even though the mother may be a highly allergic person. Cow's milk is only a substitute for breast milk and as such may present a relatively high degree of allergenicity.

The majority of babies in this country are presently fed on a cow's milk formula in one form or another and do quite well. There are also a relatively large number who suffer simple colic or become desperately ill as a result of an allergy or sensitivity to milk. For many years it has been hinted that cow's milk may disagree with some babies. Abt[1] in 1911 mentioned that some infants have an idiosyncrasy to cow's milk which produces "toxic symptoms and injuries to the baby." Piness[33] in 1925 called attention to allergic manifestation from food in infants. Pediatric textbooks barely mention milk allergy or refer meagerly to minor gastrointestinal symptoms. Several clinical reports have stressed the intestinal manifestations, omitting or barely mentioning any other type of symptoms.[27, 28, 36] The fact remains that allergy to cow's milk is a common cause of symptoms in many infants;[7, 14, 15, 43] "A formula ideal for some babies may be another baby's poison."

A critical clinical analysis of 206 infants allergic to cow's milk reveals a multiplicity of ordinary or strange, baffling, mild to serious and often apparently unrelated clinical syndromes. Various prolonged, complicated and expensive diagnostic tests, treatments and even operations have been performed in an effort to relieve these unfortunate infants, because allergy to milk was not suspected as a cause of their symptoms. The type and location of symptoms depend on two factors: (1) *the tissue or organ affected* and (2) *the results of the pathologic mechanism of allergic disease on the particular organ or tissues involved (edema of*

mucus membranes, spasm of smooth muscle and excess mucus secretion). If the allergic "trigger" area is in the nose, we may expect swelling, stuffiness and excess secretions as well as the other local and constitutional symptoms that follow. This explains why twelve clinical syndromes are described as a result of allergy to cow's milk in these infants.

Early recognition, then accurate diagnosis and treatment, are more urgent at present than in the past because of the popular tendency to avoid breast feeding in favor of cow's milk. Many infants who are contented on breast milk get minor to serious pains and problems when changed to a cow's milk formula. Cow's milk allergy in the mother is apparently not transmitted to the infant through the breast milk, although the nursing mother may herself be allergic to milk.[35] Previous studies by the author[12] and others[16, 18] have stressed the importance of early recognition and treatment of the allergic state in infants in order to prevent or minimize major allergy in later life.[13, 18] A recent convincing study by Glaser and Johnstone[21] shows four times as much major allergy developing in a control group of potentially allergic infants fed cow's milk from birth as in a similar group who were given a soybean milk substitute and no cow's milk the first nine months.[20] Our studies[13] reveal that 80 per cent of allergic infants will have major allergic symptoms as they grow older, and another 15 per cent will manifest minor allergy at one time or another. The physician should always regard milk as a possible factor in causing symptoms of disease in infants.

This clinical evaluation of 206 infants allergic to cow's milk includes immature and full term infants, males, females, white, colored and oriental. All babies were seen within the first few months of life, most of them shortly after birth, by the author. A thorough history and repeated physical examinations were performed as often as necessary to rule out other etiologic factors. The diagnosis of milk allergy was accepted when the clinical symptoms were relieved by the complete removal of milk from the infant's diet and the substitution of soybean milk (Mullsoy-Borden Co.) and when these same symptoms recurred when cow's milk was again added to the diet. If the distressing symptoms were not relieved by discontinuing cow's milk and substituting soybean milk, further studies were conducted to find the responsible factor. This group does not include babies who were on goat's milk or other milk substitutes, thirteen babies who were unable to tolerate (allergic?) soy milk, those who were not relieved while taking soybean milk, or those in whom some physical or other factor than milk allergy was proved to be the cause of the symptoms. This discussion includes *only* those infants who were almost immediately and completely relieved of their presenting symptoms when soy milk was substituted for breast milk. ***The mother's analysis and comments of immediate and complete relief for her infant are more valuable than any battery of laboratory tests.***

Distressing symptoms began in most infants at two to four weeks of age, while milk was usually the only food in their diet. One fact was fairly common in the history of almost all these unfortunate babies. The formula had been changed and juggled repeatedly (in some cases as many as eight times!) in an effort to find the magic factor. Cow's milk (and often goat's milk) modifications had been tried one after another, such as canned, evaporated, condensed, powdered, modified, fresh and acidified. The carbohydrates suffered similar acrobatics varying from sugar, refined or raw, to Karo and other syrups, dextrimaltoses, milk sugar and honey. In addition, the formulas were boiled from five minutes to five hours. Ratner[36] was among the first to demonstrate that prolonged heating lowers the antigenicity of milk and other foods. Hence some infants with mild milk sensitivity will continue to do fairly well on a milk formula, because the milk has been partially denaturized by boiling.

When milk allergy was suspected as the possible cause of symptoms, it was simpler and easier to remove cow's milk from the diet for a twenty-four to forty-eight hour trial period and substitute soybean milk than start an allergic study. This was just common sense, because the diagnosis and successful treatment were usually accomplished facts long before this type of test would have furnished additional information. Many babies were tested by scratch and intradermal methods, but often the results were indefinite.[30] No indirect or passive transfer tests were done. These tests might have provided interesting data, but they were not necessary for this type of clinical research project.

The magic factor that transformed these unhappy babies into normal infants was an animal-free milk substitute, soy milk. Hill,[23] Ratner[35] and Brown[8] have repeatedly stated that goat's milk is of doubtful value in most milk allergy patients because of the crossed reactions of the casein in animal milks. A majority of the infants who are allergic to cow's milk are also allergic to goat's milk. Many milk substitutes have been advocated and used with some success. These mixtures include taro milk,[17] meat milk[19, 29, 39] and various cereal[48] and soybean milks,[22, 46] as well as vegetable combinations.[48]

Approximately one of every fifteen infants is allergic to cow's milk to some degree, with symptoms which would not be present if these babies did not possess this peculiar sensitivity. The tendency to be allergic is bequeathed these babies by their allergic parents. The degree of intolrance or sensitivity to milk (or other allergens) varies a great deal in each individual; whereas one infant may manifest only a mild colic or "spitting up" when allergic to milk, another may collapse in shock or even die from a few drops of milk placed upon the tongue.

Soybean milk has high biologic value and provides for normal growth and development, aided by vitamin supplements, in babies. It is high in unsaturated fatty acids and supplies essential nutritional values of

protein, fat, carbohydrates and minerals.[10, 42, 47] There is no animal protein present. It is reasonable in cost, obtainable at any drug store, and easy to prepare; most infants take it readily. Sternberg[45] has shown that it maintains normal protein levels in the blood. When loose stools result from soybean milk feedings, they can often be controlled by adding one teaspoonful of Kaopectate (Upjohn) to each bottle. If soy milk is absolutely rejected by the infant, goat's milk, Nutramigen or other milk substitutes may be tried.

The age of development of the first allergic symptoms in 100 consecutive allergic infants revealed that 82 per cent exhibit their first allergic manifestations within the first four months of life, and 89 per cent by one year of age.[12] (This ratio holds true for practically all allergic babies.)

TABLE 28. *Age of Development of First Allergic Symptoms in 100 Infants*

1 Month.....39	5 Months..... 2
2 Months.....24	6–12 Months..... 5
3 Months.....13	Over 1 year.....11
4 Months..... 6	

In this group of 206 unhappy infants who were allergic to cow's milk, twelve different clinical syndromes were recognized. A detailed description of this bizarre and often paradoxical group of symptoms will be offered. The actual words and terms used by the mothers to describe the "before and after" symptoms of their allergic babies will be used. This will emphasize their peculiarity as well as their similarity to symptoms of other diseases that may sound the same. The mother's simple language is more eloquent than any scientific verbiage or chart.

The twelve groups of major allergic symptom complexes, the total number of cases and relative percentages are listed in Table 29. In each of these cases the patient was relieved of his symptoms when soy milk was substituted for cow's milk in the infant's diet. The same symptoms could be reproduced by again adding a cow's milk formula.

A majority of the infants allergic to cow's milk had several symptom groups at the same time. Two or more major symptoms occurred in about 60 per cent of the infants, while approximately 40 per cent had only one presenting symptom. Eczema accompanied by allergic pylorospasm or colic or both was the most frequent combination. The various symptoms will be described in detail.

SYMPTOMS

Eczema (Rashes)

Eczema was the most frequent symptom and was present in ninety-one cases. The lesions were usually subacute to acute, often itched, and

varied from mild to severe. The rash occurred most frequently on the cheeks, forehead and head. In other cases it was on the body, in the flexures or in the diaper area or buttocks. This type of eruption has been referred to as "heat rash," "cradle cap," "teething rash," "diaper rash," and so on. But in these particular babies the rash would dis-

TABLE 29. *Symptoms of Cow's Milk Allergy in 206 Infants*

	CASES	PERCENTAGE
Eczema	91	43
Pylorospasm	78	38
Colic	65	31
Diarrhea	47	23
"Very unhappy all the time"	40	19
Cough, croup, choking, gagging, excess mucus in throat	36	17
"Nose cold all the time"	27	13
Constipation	10	6
Asthma	15	7
"Refuses milk entirely"—anorexia	7	3
"Toxemia"—apathetic, listless, cyanotic, collapse	4	
Urticaria—angioedema	3	

appear when milk was avoided and recur on addition of a cow's milk formula in the infant's diet. Hill[24] states that eczema of all types is still the number one problem of infants, but I believe that this "honor" is to be short-lived because of the success of modern allergic management.

Pylorospasm

Seventy-eight babies with pylorospasm (persistent vomiters, "spitters," "sour babies") comprise another large and annoying group.[41] Although there are many reasons why a baby should and does vomit, these allergic infants were all relieved by avoidance of milk.[6] These "sour babies" who were "always spitting up from one feeding to the next" kept their mothers busy changing bibs, nightgowns and shirts until soybean milk was substituted for cow's milk. The baby may have only persistent "spitting up," or he may have serious projectile vomiting. This symptom, like others in this group, is usually present every day, although occasionally, for some unknown reason, the infant may skip a day. Mucus is frequently found in the vomitus, and this will show a marked eosinophilia when properly stained.[21a] Peculiarly, most of these babies gain weight, although they have a stormy course. Many have associated colic of varying degree. They may be constipated or have diarrhea, although usually the bowel movements are fairly normal. Several in this group had had complete gastrointestinal x-ray studies. Others[4, 26] have also described similar cases. Six babies had been diagnosed as having pyloric

stenosis, with classical symptoms of projectile vomiting, constipation, loss of weight, pyloric waves and marked gastric retention. Operation had been advised. Complete relief occurred, without operation, in four cases within twenty-four hours after cow's milk was omitted and soybean milk added to the diet. Two babies had pyloroplasty without relief until milk allergy was diagnosed and milk eliminated. Atropine, phenobarbital and antihistaminics were of little value in treatment.

Colic

"Colic" (belly-ache) was the real "bellyache" for sixty-five babies. This symptom was usually severe, causing "screaming" and "doubling up" and generalized discomfort which was not relieved by the usual means, such as picking him up, rubbing the back, placing him on his stomach, applying hot water bottles, or giving more food more often. These babies often cried during and after feedings and would awaken in one-half to one hour crying with "violent cramps." They would always seem hungry and were eager to eat at any time. The more often they were fed (demand feeding), the more "bellyache" they had. Many "cried, squirmed and fussed from one feeding to the next." "Spitting up" and vomiting were often present. They were "poor sleepers," passed much gas, and did not seem to be relieved by medicines. Although many had normal bowel movements, others had diarrhea and vomiting with colic. Many so-called three month colic babies deserve a twenty-four hour trial diet of soy milk to rule out milk allergy as a cause of their complaint.

Diarrhea

Diarrhea (with mucus or blood in the stool) was an annoying symptom in forty-seven infants. It was often severe, painful and persistent. It consisted of frequent, loose, watery, often curdled, yellow to green stools that irritated and burned their skin and buttocks. Mucus was usually present and in some cases was grossly visible in large amounts, which was the reason for bringing the baby to the doctor. Numerous eosinophils were present in this stained mucus.[21a, 32]

A number of babies had fairly large amounts of bright red or dark blood grossly visible in the stool, while many others had small streaks of blood. This has also been described by Rubin.[40] Colic, vomiting and occasionally dehydration occurred in the severe cases. The trypsin stool test was normal in most cases and doubtful in a few. Several infants had been previously diagnosed as having celiac disease, but the symptoms cleared up immediately on elimination of milk from the diet. Two infants in this group later actually had celiac disease. Andersen[3] states that in her series only two of eighty-seven patients with

celiac disease had milk allergy. Bloch[5, 26] describes the celiac syndrome due to food allergy. Excellent detailed monographs describing the gastrointestinal symptoms of milk allergy have recently been published by Kunstader[26] and also by Rosenblum.[37] Prolonged diarrhea following infection in the gastrointestinal tract is often present in the allergic infant.[34, 44]

"Very Unhappy All the Time"

This phrase describes probably one of the most pitiful effects of cow's milk allergy, occurring in forty infants. This simple description is the most adequate. These babies were "miserable"; "cried all the time"; "nothing makes him comfortable"; "so different from my others"; as a result of the colic, pylorospasm, rash or other symptoms from which he suffered. No old-fashioned or modern remedy would relieve these "wretched" patients, who actually looked the part, until a "miracle occurred" and they became a "changed baby" as soon as milk was removed from their diet. These unfortunate, unhappy infants are probably the counterpart of a few older children who suffer from "character changes" and are "problem children" as a result of undiagnosed, untreated or uncontrolled allergic manifestations. This has been adequately described recently by Clarke,[11] Alvarez[2] and Rowe.[38]

Chest Colds, Cough, Croup, Choking, Gagging (Excess Throat Mucus)

This hazardous group was composed of thirty-six cases and was most frequently misdiagnosed. The most serious, baffling and also most frightening symptoms relate to the lower respiratory system.[31] "My baby has had a chest cold since birth"; "he rattles all the time"; "he coughs at any time, often worse at night, and sounds croupy"; "chokes with mucus, coughs loud, coarse breathing is present almost all the time he is awake." These descriptions adequately describe this group of symptoms. Many in this group had had roentgenograms, and five babies had been treated for thymic enlargement. Two babies had undergone bronchoscopy, one of them twice. Antibiotics of all types and in large amounts had been used in most of these cases. Several had had large series of skin tests. "A miracle has taken place" were the words of a grateful mother whose nine months old infant had suffered most of the foregoing symptoms and all the treatments. This "miracle" occurred the day after the baby was given soybean milk and all cow's milk and milk products had been removed from his diet. A case report is presented to illustrate the complexities of this problem:

CASE REPORT. An infant 8 months old had had trouble in breathing since birth, characterized by a stuffy nose, persistent noisy breathing, choking, and gagging spells due to excessive mucus in his throat. When he was 6 weeks of age, his physician

discovered, by roentgenogram, a wide, upper mediastinal shadow. The baby received three deep x-ray therapy treatments for an enlarged thymus gland. The symptoms continued, and the child underwent bronchoscopy. This seemed to aggravate the condition for a few weeks. At 4 months of age bronchoscopy was again performed with apparently negative findings. At 5 months of age his physicians decided that the infant must be allergic to some food. Orange juice, pablum, fruit and vegetables were eliminated one at a time from his diet without success. At 7 months of age he was skin-tested "to many things," but the results did not furnish much positive information.

I saw him when he was 8 months old with the same symptoms of mucus in his throat, "rattling breathing," cough and nasal discharge. Physical examination revealed a normal infant except for a thick mucous nasal discharge and a moderate stridor. Smears of the nasal and pharyngeal mucus showed many eosinophils.[21a] This verified the diagnosis of an allergic condition. The mother was asked whether the baby had been taken off milk at any time, and the answer was "No." Milk was then eliminated from his diet and soybean milk was substituted. The next day the mother called and said that the child was 100 per cent better, that a "miracle" had taken place and that he seemed like a normal infant. Cow's milk was the cause of all his symptoms.

"Nose Colds All the Time!"

Nose colds that were "present from birth" occurred in twenty-seven infants. "He came home from the hospital with a cold and still has it," "just gets over one cold and has another." "His nose is always running and stuffed up so that he cannot breathe, eat or sleep well." The nasal discharge is often watery or thick, gray, shiny and stringy and contains many eosinophils when stained. The discharge persists in spite of drops, inhalations and "shots." Some infants may cough as a result of a post-nasal discharge. A night cough often accompanies the stuffy, runny, "juicy" nose. This is usually the first warning of an impending asthmatic condition. Pollen hayfever, particularly to grass, is much more frequent than present day literature would indicate. The ragweed season (in certain areas) must cause many "runny noses" and "summer colds" in babies that are undiagnosed because they are not considered allergic. Specific pollen desensitization injections give relief.

Sneezing occurred in paroxysms of three to ten times at any time of the day, although usually more often early in the morning. These babies were also found to be allergic to various inhalants as well as milk. Sneezing was often associated with the constant runny nose or "nose colds." It occurred as the only symptom in five babies in this series. Sniffling, loud nasal breathing, and stuffiness were common complaints.

Constipation

Constipation which did not respond to all the usual manipulations or oral medication was present in ten infants. The stools were usually large, well formed and hard, causing pain and tenesmus when finally passed with the aid of laxatives, enemas or suppositories. Fre-

quent and varied additions of carbohydrates, juices, fruits and malt to the diet did not relieve the condition and usually caused more colic, vomiting and general discomfort. Repeated anal dilatations also aggravated the condition. Normal stools and a happy baby quickly followed complete removal of cow's milk from the diet.

Asthma

Asthma (wheezing and cough) is not usually considered the first sign of allergy in an infant, yet it occurred in fifteen cases. The attacks were characterized by typical wheezing, loud breathing and expiratory rhonchi. It occurred more often as continuous wheezing of mild to severe degree, usually worse at night. Between actual definite asthmatic attacks some wheezing or cough occurs during each day. Many babies have a preasthmatic cough which often precedes the typical asthmatic wheeze.[9, 31] These babies have large amounts of mucus in their throats, especially while eating, and with excitement.

Anorexia

These seven infants who "fought their bottles," "refused milk" or kept "spitting out the nipple" were definitely "sickened" by the taste and feel of cow's milk. They nursed readily, rapidly and with pleasure when given soybean milk. This happy process was reversed when cow's milk was again fed these infants.

"Toxemia"

"Allergic toxemia," the most serious symptom, occurred in only four of this group of 206 infants sensitive to milk. These infants became listless and apathetic, were "limp as a wet dishcloth," may "sleep a great deal" and "seem depressed" and are actually "poisoned by milk." One baby had a grayish pallor and became cyanotic, had a convulsion and almost died on two different occasions when given milk. These critically ill infants who suffered from allergic "toxemia" or "collapse" became normal, happy babies as soon as milk was taken away from them. A case has recently been reported of death from milk allergy in a highly susceptible infant.[25]

Hives

Urticaria and angioedema were present in three infants, in mild to severe form, but quickly disappeared with elimination of milk and recurred when cow's milk was replaced in the diet.

COMMENT

General physicians (who care for 80 per cent of infants and children), as well as pediatricians, are becoming increasingly aware of the fact that an appreciable number of these patients are allergic to cow's milk.[33] Hill[23] has stressed the point that cow's milk allergy should be expected and encountered more often in infants because the first sensitivity that develops is usually to the food or foods most commonly eaten. Since milk is often the only food for the first few months, it is natural to expect some susceptible (allergic) infants to show abnormal manifestations to this food. The various groups of symptoms are characterized by their *chronicity* or *periodicity*, or both, which is the usual pattern in most allergic disease. Complete removal of cow's milk in all forms from the diet of the infant or older child is the one and only effective treatment necessary to relieve their various symptoms. It is amazing to observe how rapidly the symptoms and the illness disappear when soy milk is substituted. Since most babies allergic to cow's milk are also often sensitive to goat's milk, all animal milk should be scrupulously avoided, because of the crossed reaction to casein (protein) in animal milks.

Most of the babies in this series "outgrew" their allergy to milk within three to four months. They were then able to tolerate cow's milk in one form or another, often without difficulty. It has been stated that if a person drinks excessive quantities of milk, it might "stir up" a latent allergy to milk. This has not been our experience. We have also found no correlation between milk allergy in the infant and the amount of milk ingested by the mother prior to the birth of her baby. He usually inherits the tendency to become allergic from his parents. Glaser[21] has also noted that the infant develops an immunologic maturity about nine to twelve months of age. He then is able to tolerate some foods to which he had been allergic, provided they have been omitted from the diet as soon as allergy to these foods was noted.

NURSING MOTHER'S DIET

Certain changes in the expectant and nursing mother's diet may result in the baby's becoming "less sensitive" or less "allergic." Avoiding the highly allergic foods such as cocoa or chocolate, nuts, spices, pork and shellfish, as well as not overindulging in milk, wheat and eggs, may have a beneficial effect upon the baby. If he is destined to be allergic to milk, average or even small amounts will cause symptoms. Long boiling or exposure to high temperatures will result in milk or other foods becoming less antigenic (allergic). This explains why some infants only moderately allergic to milk will do fairly well if kept on a dried or evaporated milk formula.

Approximately 15 per cent of these patients were still unable to tolerate milk after one year of age and 5 per cent to six years of age. Many others continued to have a dislike for milk or its products. Milk is the most important food allergen in early childhood.

ALLERGIC FAMILY HISTORY

A study of the families of these 206 milk-allergic infants reveals some interesting facts: 175 had two or more allergic persons in the same family; twenty-five had two allergic parents; 168 had one allergic parent; in thirty-one there was no known family history of allergy. Eighty-five families had at least one person with a history of milk allergy. Forty per cent of milk-allergy babies have some *gastrointestinal* complaint (pylorospasm, colic, diarrhea, constipation) in addition to symptoms referable to other tissues, organs or systems.

It is evident that you cannot divorce the family history of allergy from that of the offspring. It is an important and definite part of the diagnosis.

TWENTY-FOUR TO FORTY-EIGHT HOUR DIAGNOSTIC TRIAL TEST

This is the essence of the diagnosis and treatment of milk allergy in infants. When any one or a combination of the twelve symptom groups is present and persists in spite of formula changes, medicines or other types of treatment, the infant should be given the benefit, without further delay, of a soybean milk (Mull-Soy) formula to replace completely cow's milk. A twenty-four to forty-eight hour trial feeding will quickly tell whether or not milk allergy is the major factor causing the patient's symptoms. If the baby is relieved of his symptoms, the result will be a happy baby and mother. If he is not relieved, further study and treatment are definitely indicated.

DIFFERENTIAL DIAGNOSIS

All other physical, psychologic or mechanical causes of these *bizarre* symptoms should be ruled out before a final diagnosis of milk allergy is made. Diseases of the upper and lower respiratory systems, gastrointestinal, skin and cerebral areas should be considered and ruled out by any battery of tests which may be indicated.

Every one of the 206 infants in this group was relieved of his symptoms by removal of cow's milk from his diet. Our previous studies show that 80 per cent of allergic infants will have major allergy in later life and that most of the remainder will have minor allergic symptoms. Early diagnosis and treatment may avoid, minimize or ameliorate the development or severity of allergic disease in later childhood.[18]

ALLERGY TO OTHER FOODS

Since milk is usually the only food in the infant's diet the first month or two of life, the problem of food elimination is simple. As other foods are added to the diet, more factors are involved. Any food may cause the allergic symptoms described. Wheat cereal is a frequent offender. Mixed prepared cereals should never be the first solid food because of their greater tendency to sensitize the infant. Those cereals which contain from five to ten different products are apt to initiate the first allergic manifestations more rapidly than a single cereal product that contains only one grain. Vitamins, especially the multiple preparations containing the B complex group and the natural fish oil vitamins, are common offenders. Egg should be avoided the first year; orange juice is also a frequent cause of early allergy and should be restricted till after the infant is about nine or ten months old. A new orange juice product (Bib) is less allergenic, owing to removal of the peel oil, which is apparently the main sensitizing factor in most orange juice mixtures.[38]

All new foods should be added one at a time for at least two successive days to determine whether or not they will cause undue symptoms. *Early addition of solid foods did not change, for better or worse, the tendency for the infant to become allergic to these foods.* The baby is born with this peculiar sensitivity. It may be avoided to a degree by the prophylactic measures already mentioned.

INHALANT OR CONTACT FACTORS

All the foregoing symptoms in one form or another, in varying degrees, are also caused by allergens that float in the air, are inhaled, or settle or rub onto the skin. Clothes, wool, silk, dust, feathers or other animal danders (cats, dogs, rabbits), powders, oils, fuzzy toys, insecticides, sprays, smoke and many other volatile substances, directly or otherwise, are also frequent offenders. If these factors were present in this group, they were minor factors that did not materially influence the course of the symptoms. They were definite factors in many other babies whose symptoms were not relieved by substitution of soybean milk and elimination of cow's milk. This was determined by further investigation of those infants whose symptoms continued. Cow's milk was the dominant allergen in the babies in this series of 206 cases.

Some mothers still insist that their child must drink a quart of milk a day because "it is good for him." This may be true in some instances, but can be harmful if the child has any degree of sensitivity to milk. Allergic infants are the potential hay fever, asthma and other major allergic disease patients in later life.

SUMMARY

Milk allergy is a common cause of a multiplicity of mild to severe symptoms in about 6 to 8 per cent of infants fed by artificial feeding. A twenty-four to forty-eight hour trial substitution feeding of soybean milk and complete elimination of cow's milk will quickly determine whether or not milk is the guilty factor. If the symptoms are completely relieved, the infant should be continued on soybean milk for at least four months. When milk allergy is suspected, a twenty-four to forty-eight hour trial on soybean milk is indicated.

Early recognition and proper management of milk allergy in infants may avoid and will definitely minimize serious allergic disease in the growing child. This may prevent him from becoming an "allergic cripple." He should be able to grow and develop physically and mentally as any other average child.

REFERENCES

1. Abt, I. A.: Milk as a Food for Infants. Chicago M. Rec., March, 1912.
2. Alvarez, W. C.: Puzzling "Nervous Storm" Due to Allergy. Gastroenterology, 7:241, 1946.
3. Andersen, Dorothy: Celiac Syndrome. Am. J. Dis. Child., 69:221, 1945.
4. Balyeat, R. M., and Pounders, C. M.: Pylorospasm Simulating Stenosis. South. M.J., 26:436, 1933.
5. Bloch, H.: Celiac Syndrome Due to Gastrointestinal Allergy. Arch. Pediat., 66:54, 1949.
6. Brodribb, H. S.: Vomiting in Infants. Arch. Dis. Child., 19:140, 1944.
7. Brow, R. C.: Milk Allergy in Children. Manitoba M. Rev., 27:459, 1947.
8. Brown, D. G., and Holman, R. L.: Childhood Eczema Unaffected by Goat Milk Substitutes. Brit. M.J., 1:1202, 1953.
9. Buffum, W. P.: Asthma in Infancy. Rhode Island M. J.: 33:462, 1950.
10. Cahill, W. M., and others: Digestibility and Biological Value of Soybean Protein in Whole Soybeans, Soybean Flour, and Soybean Milk. J. Nutrition, 28:209, 1944.
11. Clarke, T. W.: Relation of Allergy to Character Problems in Children. Ann. Allergy, 8:175, 1950.
12. Clein, N. W.: Significance of First Allergic Manifestations in Infants. Northwest. Med., 38:9, 1939.
13. Clein, N. W.: Growth and Development of Allergy. Ann. Allergy, 3:1, 1945.
14. Clein, N. W.: Cow's Milk Allergy in Infants. Ann. Allergy, 9:195, 1951.
15. Cohen, M.: Milk Allergy. Am. J. Dis. Child., 38:741, 1929.
16. Dees, Susan: Practical Aspects of Allergy. J. Pediat., 37:695, 1950.
17. Feingold, B. F.: Vegetable Milk Substitute; Taro. J. Allergy, 13:488, 1942.
18. Glaser, J.: Progress in Allergy: Pediatric Allergy; Critical Review of Recent Literature. Ann. Allergy, 3:373, 1945.
19. Glaser, J.: Treatment of Eczema. J.A.M.A., 137:527, 1948.
20. Glaser, J., and Johnstone, D. E.: Soybean Milk as a Substitute for Mammalian Milk in Early Infancy. Ann. Allergy, 10:443, 1952.
21. Glaser, J., and Johnstone, D. E.: Prophylaxis of Allergic Disease in Newborn. J.A.M.A., 153:620, 1953.

21a. Hansel, F. K.: Clinical Allergy. St. Louis, C. V. Mosby Company, 1953, p. 411.

22. Hill, L. W.: An Evaluation of Therapy in Infantile Eczema. J.A.M.A., *140*:139, 1949.
23. Hill, L. W.: Eczema in Infancy and Childhood. New England J. Med., *242*:286, 327, 1950.
24. Hill, L. W., and Stewart, R. E.: Soybean Food Preparation for Feeding Infants with Milk Allergy. J.A.M.A., 39:985, 1929.
25. Kelvin, C. B.: Death in a 6 Day Old Infant. J. Pediat., *33*:457, 1948.
26. Kunstadter, R.: Gastro-intestinal Allergy and the Celiac Syndrome. J. Pediat., *21*:2, 193, 1952.
27. McGee, W. A.: Colic: Its Pattern in Infancy. South M.J., *43*:335, 1950.
28. McLendon, P. A., and Jaeger, D. S.: Milk Intolerance—Cause of Nutritional Entity. South. M.J., *36*:571, 1947.
29. McQuarrie, I., and Ziegler, M. R.: Comparison of Nutritive Value of Mineral Enriched Meat and Milk. Pediatrics, 5:210, 1950.
30. Matheson, A.: Personal communication.
31. Nance, F. D.: Asthma in the Newborn, or "Doctor—Is It Thymus?" Hawaii M.J., *6*:400, 1947.
32. Nance, F. D.: Stool Eosinophilia in Gastrointestinal Allergy of Infants. J. Pediat., *33*:313, 1948.
33. Piness, G.: Allergic Manifestations in Infancy and Childhood. Arch. Pediat., *42*:557, 1925.
34. Rappaport, E. M.: Allergy Causing Post Dysenteric Diarrhea. Rev. Gastroenterol., *15*:466, 1948.
35. Ratner, B.: Treatment of Milk Allergy and Its Basic Principles. J.A.M.A., *105*:934, 1935.
36. Ratner, B.: Management of Preallergic Child. Ann. Allergy, *6*:629, 1948.
37. Rosenblum, A. H., and Rosenblum, P.: Gastro-intestinal Allergy in Infants. Pediatrics, 9:311, 1952.
38. Rowe, A. K.: Food Allergy, J. Allergy, *1*:172, 1938.
39. Rowe, A. K.: Food Allergy. Philadelphia, Lea & Febiger, 1944.
40. Rubin, M. I.: Allergic Intestinal Bleeding in the Newborn. Am. J. M. Sc., *200*:385, 1940.
41. Schoenkerman, B. B.: Allergic Aspects of Recurrent Vomiting in Infants. Exhibit, Annual meeting, American College of Allergists, Chicago, 1952.
42. Schroeder, L. J., and others: The Utilization of Calcium in Soybean Products and Other Calcium Sources. J. Nutrition, 32:413, 1916.
43. Sobel, S. A.: Milk Allergy in a Case of Triplets. Clin. Med., 59:362, 1952.
44. Speer, F.: Role of Allergy in Infectious Diarrhea of Infancy. J. Kansas M. Soc., Nov., 1952.
45. Sternberg, S. D., and Greenblatt, I. J.: Serum Protein Value in Infants Fed Soy Milk. Exhibit, American College of Allergists, Chicago, 1951.
46. Stoesser, A. V.: Clinical Evaluation of Soybean Food in Eczema of Children. Ann. Allergy, 2:404, 1944.
47. Stoesser, A. V.: Influence of Soybean Products on the Iodine Number of the Plasma Lipids and the Course of Eczema. J. Allergy, *18*:29, 1947.
48. Wolpe, L. Z.: Treatment of Infantile Eczema with Milk Substitutes. Arch. Pediat., *64*:399, 1947.

1155—10th Avenue North
Seattle 2, Washington

LOCAL TREATMENT OF ATOPIC DERMATITIS

LLOYD S. NELSON, M.D.

ALBERT V. STOESSER, M.D.

There is no single form of local treatment of eczema. The success of any form of management depends upon the completeness of the allergic history and the ability to avoid excitants, both ingested and inhaled, and contactants The parents must be thoroughly oriented in the care of the allergic child. The treatment of these patients requires detailed instructions and meticulous adherence to diet and environmental control. The parents must be adequately informed regarding the course of eczema. In the infantile age group there is a natural tendency for the subsidence of the eczema and a shift to a respiratory form of allergy. The possibility of exacerbations and remissions of the disease while under treatment must be explained. If more time were spent in orientation, there would be less "shopping around" from one doctor to another. These patients are often handled by a defeatist attitude on the physician's part, which is quickly grasped by the parents. If the parents are carefully informed, better cooperation will prevail and ultimately more satisfactory results will be attained. Most eczematous patients can be made more comfortable, and a few can be cured. In this paper principles of local care to the skin and practical features of treatment will be stressed.

GENERAL PRINCIPLES OF TREATMENT

The eczematous child must be protected from certain allergens in his environment. Some of these materials can produce exaggeration of the existing eczema by direct contact or by inhalation. The transepidermal penetration of some allergens such as egg is believed to occur.

From the Department of Pediatrics, University of Minnesota Medical School.

Highly irritative agents, such as strong soaps and bleaches, used to launder patients' garments and bedclothes must be eliminated. Woolen clothing and blankets should be substituted by cotton or nylon whenever possible. There are available heavy cotton-lined garments with glass wool filling for outdoor clothing. They are suitable for patients living in cold climates.

House dust control, particularly in the bedroom, is a necessity regardless of which antigens the skin tests would signify. Animal pets should never be allowed in the eczema patient's environment. Toys should be wood, rubber or plastic. Eliminate the stuffed variety. Feathers must be excluded from the child's surroundings.

Eczematous children often improve dramatically upon hospitalization. Improvement may result from better environmental control. Consequently the child with eczema should have his own room, which ought to be furnished only with a bed, dresser and washable curtains. Floor coverings are not encouraged unless removable cotton rugs are used. Daily damp moppings are indicated.

Room temperature should be maintained at a comfortable level. Overheating produces perspiration and more itching. Chilling is certainly not desired.

SKIN CARE

The infant's and young child's skin is particularly prone to irritation. Ordinary soaps may act as irritants to the child with eczema. This irritating property may be due to the alkalinizing effect of soap and builders, to irritating fatty acids, dyes, preservatives, perfumes, bleaches, germicides and medicinal agents. Allergists have recognized these irritating factors and have sought substitutes for soaps as cleansers.

The use of cleansing oils and demulcents has not proved satisfactory. These agents predispose to secondary pyogenic infections. There are now available several soapless synthetic detergents which are satisfactory for skin cleansing. Two of these liquid preparations, Acidolate and Phisoderm, are fairly satisfactory. The detergent sodium lauryl sulfate, now available in cake form (Lowila), has proved a most valuable adjunct in the care of the skin.

These agents, in addition to their cleansing action, are also germicidal. It must be cautioned, however, that too frequent washings with even these hypoallergic cleansers is not recommended, since they produce a drying effect on the skin.

Frequent bathing of these children should be discouraged, because flare-ups in the eczema may occur. In the subacute or chronic stage of eczema the skin is already dry, and the degreasing effect of all cleansers may be harmful.

MEDICAL TREATMENT

The local treatment of atopic eczema depends entirely on the stage of the eczematous process. These may be divided into acute, subacute and chronic stages. In each group, therapy is governed by the presence or absence of secondary infections.

Acute Stage

The acute stage of eczema can further be divided into acute exudative and simple acute eczema.

Acute Exudative Eczema. In the acute exudative form there is a marked erythema with weeping. For these patients the use of moist packs is satisfactory. Burow's solution diluted 1:20 to 1:30 is helpful. Potassium permanganate, 1:5000 to 1:10,000, is particularly useful when mild secondary infection is present. When infection complicates the eczematous skin, wet dressings can be prepared by dissolving one of the antibiotics in normal saline solution. Neomycin has greater stability than the other antibiotics and is prepared so that 2 mg. of it are present in each cubic centimeter of the isotonic saline solution. This agent is particularly effective against staphylococci. Terramycin prepared in such a way that 1 mg. of this antibiotic is present in 1 cc. of normal saline solution is also effective against the staphylococci, streptococci and some gram-negative bacilli. For a few children, painting the weeping areas with 2 to 4 per cent gentian violet has been beneficial. The routine use of boric acid moist compresses should be condemned. This is a poor antiseptic agent, and the absorption from the skin may be sufficient to produce boron poisoning.

The use of moist packs is chilling, particularly to the young patient, but adequate warmth can be attained by use of a light cradle. In most cases better results are attained by keeping packs on only for alternate hours.

Simple Acute Eczema. In simple acute eczema the skin is in the papulovesicular stage and has not progressed to the weeping stage. In these patients lotions and some ointments are helpful. The following formulas are recommended:

Cetaphil lotion ..... 120.0 cc.

Prepared calamine ..... 8.0 gm.
Starch ..... 24.0 gm.
Glycerin ..... 0.1 cc.
Liquid phenol ..... 0.1 cc.
Distilled water q.s. ..... 120.0 cc.

Calotex (with or without
0.25 to 0.5 per cent phenol) ..... 120.0 cc.

Burow's solution ..... 20.0 cc.
Velvachol ..... 20–30 gm.
Zinc paste (Lassar's) q.s. ..... 60 gm.

Domeboro ointment or Hydrosol ..... 60 mg.

The first time any ointment is prescribed, parents are instructed to apply it only to one small area and observe for a day for possible reaction. Whenever a cream or an ointment is used, instructions must be given to use the preparation frequently as a thin layer. Multiple application is indicated because the child easily rubs off the medication. This may necessitate ten to fifteen thin applications daily. In resistant patients, parents are instructed to apply ointments first to porous gauze and then place this gauze lightly in position. The method of applying ointments to cellophane or waxed paper and then to the skin enhances perspiration and produces more itching. Therefore the method is not recommended.

A few of these patients are made more comfortable by use of colloidal or tar baths.

If a secondary infection is present, Terramycin ointment, Neomycin cream or Vioform, 3 per cent, incorporated in an absorbent base is valuable.

Subacute Eczema

In this stage of eczema there is crusting and some papulovesiculation, but no weeping. Itching is usually intense, and excoriations with secondary infection are common. The secondary infection must be cleared up first. Terramycin or Neomycin creams or ointments are successful. Vioform is available as a cream and ointment and is most helpful. The ointment bases work better than the creams when crusting is pronounced.

When infection is absent, the following preparations have given good results:

Crude coal tar ..... 0.5–1 gm.
Burow's solution ..... 10.0 cc.
Heavy emulsion base ..... 20.0 gm.
Zinc paste (Lassar's) q.s. ..... 60.0 gm

Crude coal tar ..... 0.5–1 gm.
Zinc oxide ..... 12.0 gm
Amyli ..... 12.0 gm.
Almay qualatum ..... 12.0 gm.
Velachol q.s. ..... 60.0 gm.

Ultar ..... 60.0 gm.

Kolpix "A" ..... 60.0 gm.

Va-Tar "A" or "B" ..... 60.0 gm.

Juniper tar ointment ..... 60.0 gm.

These preparations are usually well tolerated, but occasionally an infant or young child will react to any tar preparation. In these instances the following may be tried:

Zinc oxide ..... 12.0 gm.
Amyli ..... 12.0 gm.
Almay qualatum q.s. ..... 60.0 gm.

Naftalan ..... 3.0 gm.
Menthol ..... 0.06 gm.
Burow's solution ..... 15.0 cc.
Velvachol ..... 15.0 gm.
Zinc paste q.s. ..... 60.0 gm.

Ichthyol ..... 2.0 gm.
Naftalan ..... 10.0 gm.
Aquaphor ..... 20.0 gm.
Zinc paste q.s. ..... 100.0 gm.

Naftacol ..... 60.0 gm.

A great number of antihistaminic ointments have been developed. Their effects have been unsatisfactory except as local anesthetics. Cortone and Hydrocortone ointments have been marketed with great enthusiasm for the eczematous patient. In most cases the results with these agents have been disappointing.

Chronic Eczema

In the chronic type the common sites are the antecubital and popliteal areas, wrists and posterior portion of the neck. There is no weeping and rarely any vesiculation. Papulation and later lichenification are common. Many children have dry skins, and response to treatment is often discouraging.

The most effective agent in this group of patients is tar. When only small patches of eczema are present, the use of Tar dermament or 10 per cent crude coal tar in a solution of equal parts of acetone and collodion applied once daily is helpful. When the disease is more extensive, 1 to 5 per cent tar in Lassar's paste can be applied.

The possibility of damage to the kidneys by tar preparations must be remembered, and urine examinations should be done regularly in all patients upon whom tar is being applied. There are occasions when a wood tar will produce prompt healing when coal tar has been ineffective.

Softening ointments such as Aquaphor, Hydrotex, Velvachol and Dermabase help to maintain the skin in a healthy state.

In order to have success from topical therapy, trauma must be reduced. Cuffs are used to prevent flexing at the elbow and scratching

of the face. In some instances further restraints are temporarily necessary. The arms and legs are then held outstretched by means of strips of cloth extending from the wrists and ankles to the bars on the crib. The skin at the wrist and ankle is first well protected with cotton. If the child rubs the face on the bedclothes, a sheet of heavyweight plastic material can be used. A piece about 2 feet square is fastened to the bed under the infant's head by strips of adhesive tape. Small infants should not be allowed to remain in restraints for long periods, because respiratory secretions tend to collect and the possibility of pneumonia must be considered.

The eczematous child is uncomfortable, and itching is present in nearly all cases. Antipruritics such as menthol, 0.25 per cent, camphor, 0.5 per cent, or phenol, 0.5 to 1 per cent, incorporated in the local medicament are helpful. In many cases sedatives are needed to make the child comfortable. Chloral hydrate by mouth or rectum in 5- to 10-grain doses is valuable. Several preparations of oral chloral hydrate such as Somnos of Sharpe and Dohme and Noctec of Squibbs are obtainable. Chloral hydrate supprettes of William Webster Company are available in 5, 10, 15 and 20 grain sizes.

The topical application of antihistaminic ointments is valuable only as local anesthetic agents. The oral preparations of Histadyl, Decapryn and Benadryl have been helpful in some patients. This effect may be due primarily to sedation, and adding small amounts of barbiturates to these preparations enhances their value. Aspirin in small doses will control itching in some children.

The cleaner the child's environment and the more intelligent and enthusiastic the parents, the better the results from present day methods of treatment of atopic dermatitis.

616 LaSalle Building
Minneapolis 2, Minnesota

ACTH AND CORTISONE IN THE TREATMENT OF ATOPIC DERMATITIS

JAMES C. OVERALL, M.D.

The indications for and the general principles of the clinical use of ACTH and cortisone in the treatment of infantile eczema (atopic dermatitis) are on a much more definite basis now than when they were first used for this condition about four years ago. This paper will be confined largely to the practical use of these hormones. If one desires a more detailed analysis of the physiology, pharmacology, side reactions, and so on, reference can be made to numerous reports.[8, 10-13, 17, 18]

It is now generally recognized that these hormones do not cure, but only temporarily relieve the symptoms of some of the manifestations of allergy. In general, they affect a group of diseases in which it is not the known or unknown etiologic irritant, but the reaction of the tissues to the irritant (in allergy the antigen), that constitutes the disease. ACTH stimulates the adrenal cortex in both hyperplasia and secretion —mainly to produce 17-hydroxy-corticosterone (Compound F) and, to a less extent, 17-hydroxy-dehydrocorticosterone (cortisone, or Compound E) and a total of twenty-six other steroids. This stimulation produces an excess of the hormones, the use of which cannot be compared with that of insulin in diabetes and thyroid in cretinism, since both of these are, of course, substitution therapy.

Therapy with ACTH and cortisone, although it may be productive of immediate benefit, may also be harmful. This is especially true if cortisone is used over a long time, when the danger of decalcification of the skeleton and pathologic fractures has been shown by Irwin and co-workers.[3] In certain conditions, however, in which the symptoms are self-limited or of short duration, intensive administration may be

indicated and in some few instances apparently lifesaving—e.g., severe drug reactions with hemorrhage and exfoliative dermatitis, as well as any other condition in which severe stress and shock are present. Cortisone seems to act as a buffer to the disease toxin or irritant, yet does not seem to affect the antigen-antibody reaction (blocking or sensitizing) or the formation of histamine.

ACTH has no or only slight effect on the allergic skin tests.[1, 4, 7] The buffer action of these steroids is probably at the cell level or within it and, while the hormone is being given, protects the cell. If the causal irritant or antigen can be found and removed while this protection is present, the clinical improvement will continue. If the hormones are given in the presence of an infection, there is no inhibition of, but rather a masking effect on, the growth of the organisms.[5] Therefore, of necessity, full doses of appropriate antibiotics must be used if infection is suspected. ACTH and cortisone will interfere with the proper evaluation of trial or elimination diets, environmental control and other similar clinical observations.[14] Their action does, however, give the patient such a sense of well-being and relief from fever, pain and other symptoms that he may feel he is well. If the drug is continued over a long period, this feeling of exuberance can, but rarely does, lead to habit formation similar to that seen in opiate addiction.

PRINCIPLES OF TREATMENT

In making recommendations for the use of these hormones in atopic dermatitis it is suggested that they be used only as a temporary expedient in (1) severe acute or chronic uncontrolled eczema—as in severe status asthmaticus—when routine or ordinary measures have not helped or when one may even be concerned about the patient's life; (2) moderately severe chronic eczema, when some relief may have been obtained, but not sufficient to allow for a complete "allergic work-up," when ACTH or cortisone can be used until routine treatment will again bring relief. A typical example would be failure of wet soaks plus other routine measures to alleviate the constant oozing and itching.

Although ACTH and cortisone, when used in proper dosage, have brought relief to a high percentage of cases,[2, 6, 7] they should not be used as the first treatment, but probably only as the last. It is still necessary to carry out the usual detailed allergic, pediatric and dermatologic management. The first treatment should be diagnostic, to determine whether the skin condition really is atopic dermatitis and not some other frequently confused but similar skin eruption.

One of the most common errors is to misdiagnose seborrheic dermatitis (also called "cradle cap") in infants. Here, however, a careful history showing the onset of the rash on the scalp, plus the greasy, scaly

appearance and the usually rapid response to 1 to 2 per cent salicylic acid in petrolatum or 2.5 per cent ammoniated mercury ointment will in some instances clear up the rash and the diagnosis.

At times ordinary contact dermatitis can be difficult to differentiate. In this instance a therapeutic trial of eliminating the most likely irritants, as determined by a careful history, plus the judicious use of some bland cream or lotion should relieve the condition or bring one face to face with the atopic eczema problem.

Parasitic, fungous or pyogenic infections can occasionally give trouble, but appropriate and specific medication should bring about prompt clearance and eventual cure.

Before starting treatment one must make sure that certain contraindications are not present. These contraindications are as follows: nephritis and/or hypertension, diabetes mellitus, tuberculosis (and syphilis?), severe emotional imbalances and psychotic states, certain cardiac lesions with low reserve (congestive failure), peptic ulcer or any possible gastrointestinal bleeding, sepsis. If any of these conditions is present, definite precautionary measures must be taken.

Certain precautions should also be exercised during the actual treatment. (1) Hospitalize a patient for ACTH administration. (2) Weigh the patient at the onset and daily or at least semiweekly. (3) Take the blood pressure daily or at least semiweekly. (4) The sodium intake should be low (less than 1 to 2 gm.), and the potassium intake should be increased (add 1 to 3 gm.). (5) Determine the total eosinophil count before commencing therapy and at intervals during therapy. (6) Administer antibiotics routinely when any possible infection is present.

DOSAGE OF ACTH AND CORTISONE

The dosage varies more with the severity of the condition than with the age or weight of the patient and also seems to vary from patient to patient even with the same clinical picture. Infants require (as with many other drugs) a larger dose per kilogram than do adults. Hill[9] arbitrarily recommends 25 mg. of cortisone every eight hours. In general, the dose of ACTH varies from 5 to 25 mg. intramuscularly every six hours or 2 to 10 mg. intravenously given in 5 per cent glucose solution by a slow (20 to 30 drops a minute) drip over a six or eight hour period. The intravenous route will certainly give quicker and as good or better results and is especially useful in the severe acute case. The intravenous route should be followed by intramuscular injection, but on slowly reducing dosages; in fact, it is variously estimated that the intravenous route requires one fifth to one twentieth of the intramuscular dose.[4, 16] Thorn[16] has shown that nearly maximal stimulation is obtained with 1 to 2 units (mg.) an hour intravenously and that as little as 0.25 unit

an hour will cause a fall in the eosinophil count and an increase in 17-hydroxycorticoids. A drop in eosinophils is no absolute criterion of success, however, for good clinical results have been obtained without any change.

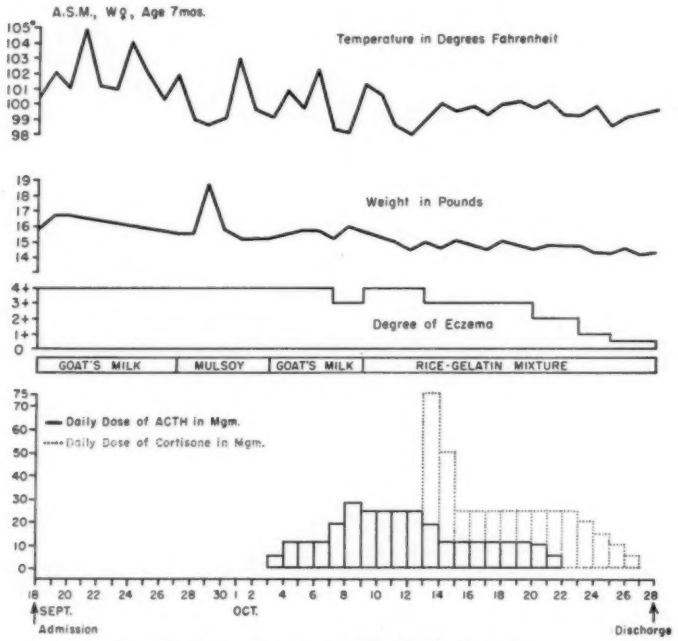

Fig. 32. Chart of patient with infectious eczema.

When ACTH is used over an appreciable time and then suddenly withdrawn, a "let-down" will occur. Following with cortisone in small and decreasing doses will help prevent this. The largest intravenous dose used in my experience was 40 mg. over an eight hour period in a thirteen year old girl with disseminated lupus erythematosus without any ill effects.

The daily dose of cortisone varies from 25 to 200 mg. given in four equal amounts every six hours orally, or once daily intramuscularly. The oral dose is usually effective and is, of course, preferred by the patient. As soon as a good clinical response has been obtained, gradual reduction of the amount is indicated. Cortisone has a cumulative effect which frequently lasts for a few days after its withdrawal and depresses the function of the adrenal cortex. This makes the use of one or more small stimulating doses of ACTH indicated upon its sudden withdrawal.

CASE REPORT

The following report of one of the first cases treated illustrates some of the early difficulties and errors in treatment.

S.M., an adopted 7 months old white female infant from a town 50 miles from Nashville, was admitted to Vanderbilt University Hospital September 15, 1950, with severe intractable and infected eczema. There had been no appreciable response to numerous changes in local as well as dietary treatment by the family physician and by a pediatrician. A generalized reaction requiring epinephrine had occurred when a mixed cereal was added to the diet.

On admission wet soaks were used, and penicillin, streptomycin, Aureomycin and Gantrisin were given to combat a sepsis (blood culture was twice positive for Pseudomonas). After 10 days of antibiotics, 1 per cent acetic acid locally (crusty, infected skin lesions showed green pus) and transfusions the infection was brought under control—but not the eczema. ACTH was started and increased from 12 to 25 mg. a day. Then cortisone, 75 mg. a day, was substituted; this dose was reduced slowly to 50 mg. and then to 25 mg. and finally, after slowly reducing the doses, stopped. Whether because of the hormones, dietary changes, local treatment or all combined, the skin cleared somewhat. After 6 weeks in hospital the patient was discharged, only to have a relapse again in 2 weeks. A local physician started her back again on cortisone with slight temporary improvement.

Two months later the patient returned to the Vanderbilt Out-Patient Department, weighing 12 pounds and 6 ounces (her previous hospital admission weight had been 15 pounds and 13 ounces and rose in the hospital to 16 pounds and 11 ounces). She had severe generalized eczema and was again put on cortisone plus general measures. A few days later we learned from the family that the baby had died, possibly from sepsis, since antibiotics were apparently not continued.

REFERENCES

1. Burrage, W.: Effect of ACTH on Immediate Skin Reaction and Passive Transfer Test in Man. J. Allergy, 22:99, 1951.
2. Callaway, J. L.: ACTH and Cortisone: Their Role in Dermatologic Therapy. South. M.J., 45:63, 1952.
3. Editorial. J. Allergy, 25:190, 1954.
4. Feinberg, S. M., and others: ACTH and Cortisone in Allergic Manifestations. J. Allergy, 22:195, 1951.
5. Finland, M., and others: Effects of Adrenocorticotropic Hormone in Pneumonia. Ann. Int. Med., 33:1081, 1950.
6. Glaser, J.: Treatment with ACTH and Cortisone of Atopic Dermatitis (Eczema) in Infants and Children. J. Allergy, 23:222, 1952.
7. Glaser, J., and others: Experiences with ACTH and Cortisone in Treatment of Asthma and Eczema in Infancy and Childhood. Ann. Allergy, 9:292, 1951.
8. Hampton, S. T.: Clinical Use of ACTH and Cortisone in the Treatment of Allergic Diseases. South. M.J., 45:1061, 1952.
9. Hill, L. W.: Oral Cortisone in the Treatment of Infantile Eczema. New England J. Med., 248:1051, 1953.
10. Kinsell, L. W.: Clinical Application of ACTH and Adrenal Steroid Hormones. Ann. Int. Med., 35:615, 1951.
11. Means, J. H.: Endocrine Function. Ann. Int. Med., 34:1311, 1951.
12. Proceedings of the First Clinical ACTH Conference. Philadelphia, Blakiston Company, 1950.
13. Proceedings of the Second Clinical ACTH Conference. Philadelphia, Blakiston Company, 1951.

14. Rowe, A. J., and Rowe, A. H.: Cortisone and Corticotrophin in Allergic Disease. California Med., 77:387, 1952.
15. Stone, R. E., and Spies, T. D.: ACTH and Cortisone as Therapeutic Agents. South. M.J., 45:885, 1952.
16. Thorn, G. W.: Intravenously Administered ACTH. New England J. Med., 244:796, 1951.
17. Thorn, G. W.: The Adrenals in Health and Disease. Tr. & Stud., Coll. Physicians, Philadelphia, 19:95, 1952.
18. Thorn, G. W., and others: The Clinical Usefulness of ACTH and Cortisone. New England J. Med., 242:783, 824, 865, 1950.

1924 Church Street
Nashville 3, Tennessee

MANAGEMENT OF THE ACUTE ASTHMATIC ATTACK IN CHILDHOOD

SAMUEL J. LEVIN, M.D.

ENVIRONMENT

The child with an acute attack of asthma should be put to bed in a room kept at an even temperature of about 70° F. Recovery is much faster when there is less demand on the pulmonary system. If there is an associated respiratory infection, resolution will occur more rapidly if the patient is in bed, where fluctuations in room temperature and drafts are more easily avoided. A reasonable amount of fresh air should be admitted. Most asthmatics are aggravated by house dust and lint, either allergically or mechanically. For this reason the bedroom should be kept as dust-free as possible.

The following precautions should be rechecked during the attack: the mattress, box spring and pillows should be enclosed in dust-proof covers; quilts, comforters, chenille bedspreads and all fuzzy items, including stuffed animals and toys, should be eliminated. The best cover for the allergic child is a woollen blanket *completely* enclosed in a blanket cover of broadcloth or sheeting. Coarse woollen particles cannot penetrate such a cover. The floor should be bare except for a few small, smooth, washable cotton throw rugs. It is much better to oil the floor with a mixture of mineral oil and furniture polish, equal parts, than to wax it. This traps any dust that might settle. Hot air outlets should be covered with several layers of gauze or with filters. In addition, a room air-conditioning unit may be helpful in the summer to reduce the temperature and the humidity, as well as to produce a lower pollen content in the room should pollen be an etiologic factor in the attack. Smoking should be interdicted in the child's room. Smoke is harmful to every asthmatic patient, either allergically or as a chemical irritant.

From the Allergy Clinic of the Children's Hospital of Michigan, Detroit.

Parents and attendants must be cautioned not to smoke in the child's vicinity or in the automobile while transporting the child. Many asthmatics feel better when there is movement of air in the room such as that produced by a slowly revolving fan 8 to 12 feet from the child's face. The patient will feel more comfortable propped up in bed on several pillows, which should be enclosed in nonallergic covers. Foam-rubber pillows are useful except that there is some recent evidence to show that molds may grow in such material. For this reason nonallergic covers are still the best solution to the bedding problem.

In the presence of a respiratory infection producing an associated laryngitis, tracheitis or bronchitis, steam inhalations are helpful to thin out secretions and allay coughing. In our experience plain steam accomplishes as much as medicated steams with less likelihood of irritation to the respiratory passages due to the medicaments used. We have found a steam kettle kept boiling continuously in the room of value between inhalations.

DIET

During an acute attack of asthma the diet should be light. Cold foods and drinks should be eliminated. The attack can be prolonged and aggravated by the feeding of ice cream, cold custards, cold milk and similar cold foods and liquids. The most important elements of the diet during the attack are water and sugar, which should be pushed. There is normally a loss of appetite during the attack. Sweet liquids such as tea, fruit juices and soft drinks at room temperature should be offered frequently. Sugar intake must be kept up to overcome the tendency to acidosis, so easily induced in many of these patients. At the onset of the attack a mild cathartic is often useful. During this period all foods should be eliminated to which there has been a suspicion of sensitivity. It is often found that the child's tolerance to many foods to which there is definite sensitivity may be good between attacks. During the attack many of the items previously well tolerated may aggravate the symptoms. During the acute attack of asthma many children become nauseated, and some have severe vomiting. Some patients have in addition abdominal pain. For this reason it is wise, in this type of case, to interdict milk at the very onset of the attack. In our experience, milk during the attack of asthma, in children subject to nausea and vomiting, definitely aggravates this tendency.

USEFUL DRUGS

Nose Drops

Nasal congestion is often present in the prodromal stages of asthma and may be allergic or infectious, or both. A decongestant nose drop

should be started at once so as to obviate mouth breathing. Air passing through the nose is warmed and moistened and is more agreeable to the sensitive bronchial mucosa. An efficient nose drop which has superseded almost all others in our practice is N.T.Z. (Winthrop-Stearns), containing the following ingredients:

Neo-synephrine, 0.5% (a decongestant)
Thenfadil hydrochloride, 0.1% (an antihistaminic)
Zephiran hydrochloride 1:5000 (a wetting and antibacterial agent)

These drops are singularly effective for nasal congestion due to either allergic or infectious causes. In several hundred patients we have observed no deleterious effects from their frequent and prolonged use.

Cough Medicine

Suitable medication for cough should be ordered for use early in the attack. Such a prescription should contain codeine and ephedrine hydrochloride, 8 mg. (⅛ grain) of each per teaspoon. A suitable vehicle containing syrup acid hydriodic or a guiacol preparation for their expectorant action is helpful. A typical prescription follows:

Codeine phosphate . . . . . 0.2 gm. (3 grains)
Ephedrine hydrochloride . . . . . 0.2 gm. (3 grains)
Syrup acid hydriodic . . . . . 30 cc. (1 oz.)
Syrup cocillana compound, q.s. . . . . 90 cc. (3 oz.)
½ to 1 teaspoonful every three to four hours

A guiacol preparation such as Syrup Thiocol (Roche) is a good alternate for the hydriodic syrup in patients with a dry, nonproductive cough. There are many proprietary cough preparations available containing various combinations of an antihistaminic and an expectorant, with or without codeine. Some contain ephedrine. All may be useful in selected cases.

Codeine should be used judiciously in cough prescriptions. The physician should be on guard for symptoms of overdosage or idiosyncrasy to codeine such as itching around the nose and mouth, a tendency to drowsiness and depression of the respiratory rate.

Ephedrine Preparations

Ephedrine preparations orally are useful, provided no side effects occur. The dose varies from 8 to 25 mg. (⅛ to ⅜ grain). Some children become extremely drowsy on small doses of ephedrine. Two patients in our practice, one five, the other seven years of age, had severe narcosis and slept as if anesthetized for almost twenty-four hours after 25 mg.

(⅜ grain) of ephedrine orally. Other children are overstimulated by ephedrine. Nausea and vomiting also occur with this drug. We have found ephedrine hydrochloride less likely to produce gastrointestinal irritation than the sulfate. Propadrine hydrochloride in doses of 8 to 30 mg. (⅛ to ½ grain) is a good substitute for children who cannot tolerate ephedrine. Many useful proprietary preparations are available combining a barbiturate with ephedrine. Others contain, in addition, aminophylline. All are useful in selected cases. Among the most popular is Tedral (Maltine Company), containing:

Phenobarbital	8 mg. (⅛ grain)
Aminophylline	130 mg. (2 grains)
Ephedrine	25 mg. (⅜ grain)

The dose is ½ to 1 tablet, depending on the age of the patient and the severity of the asthma. One must remember that any of these ingredients may produce side reactions.

Syrup of Ipecac

In our opinion this old-time remedy is more popular than it merits. It is used by some practitioners during the early stages of the attack to induce vomiting and so loosen and expel the mucous plugs in the bronchial tree. We never use it, since we are fearful of uncontrollable vomiting and subsequent ketogenic acidosis, which is all too easily induced in some asthmatic children. This may become a more difficult problem to manage than the asthma itself. The dose of syrup of ipecac, should one wish to use it, is 5 drops for an infant one year old. One drop is added for each additional year. This is repeated every fifteen minutes until vomiting occurs.

Epinephrine Hydrochloride

Aqueous epinephrine (1:1000) hypodermically is still the drug of choice for the treatment of an acute attack of asthma. It is much better to give children small amounts frequently rather than large doses at wide intervals. Many children get severe pallor and nausea, sometimes accompanied by shocklike symptoms, from overdosage with epinephrine. Injections of 0.1 to 0.25 cc. (1½ to 4 minims) of the 1:1000 solution may be repeated every two to four hours if necessary. The best dose is the smallest one that will give relief without undesirable side reactions. We have found that much of the apprehension and anxiety in both patient and parents can be prevented by our practice of teaching the parents the technique of the hypodermic administration of the proper dose of epinephrine early in the attack.

In certain cases slow-acting epinephrine may be of considerable value alone or after an initial dose of the aqueous epinephrine 1:1000. Until recently we occasionally used epinephrine in oil, 1:500, in doses of 0.25 to 0.5 cc., depending on the age of the child and the severity of the attack. During the past few years we have had considerable experience with, and have been favorably impressed by, the action of an aqueous suspension of epinephrine, Sus-Phrine 1:200 (Brewer). This material has a decided advantage over epinephrine suspended in oil. There is no difficulty with this material in obtaining an even suspension with a few shakes of the ampule even if it has been standing for a considerable time. The aqueous suspension flows freely through an ordinary hypodermic needle. Another advantage is that 20 per cent of the amount injected is available for immediate bronchodilator effect. The balance is gradually liberated for sustained action. We have given doses of 0.1 to 0.25 cc. (1½ to 4 minims) to children, with excellent immediate as well as prolonged effect.

Bronchodilators

Bronchodilators by inhalation may be useful in older children. We have rarely found children under seven or eight years sufficiently cooperative to derive much benefit from this procedure. However, by using a motor-driven pump and a special mask, aerosolized epinephrine can be administered at any age, but in our experience the results are hardly worth the special apparatus required. Epinephrine hydrochloride 1:100 prepared for inhalation is the most commonly used preparation. Among others which are also effective are Isuprel 1:200 (Winthrop-Stearns), Aeroline Compound (Lilly) and Vaponefrin (Vaponefrin Company). An efficient all-glass (or all-plastic) nebulizer must be used with these solutions to obtain a fine aerosol. We can recommend as among the most efficient the DeVilbiss number 40 regular size or number 41 pocket size nebulizer.

Sedation

Morphine should never be used in the treatment of asthma in either children or adults. The barbiturates are safe and should be used freely to control apprehension and to give the child sufficient rest. Nembutal (sodium pentobarbital—Abbot) or Seconal (sodium secobarbital—Lilly) can be given orally in doses of 50 to 100 mg. (¾ grain to 1½ grains). Larger doses are required when barbiturates are given rectally either by suppository or in ½ ounce of tap water as a retention enema in patients who are vomiting. Children have a high tolerance for barbiturates, and larger doses per pound of body weight than for adults

are required. Hypodermic administration of sodium phenobarbital, 30 to 60 mg. (½ grain to 1 grain), is occasionally necessary.

Antihistaminics

The antihistaminics are sometimes useful in asthma, but rarely if the attack is accompanied by a respiratory infection. There is no antihistaminic universally successful in any of the allergic diseases. Although most patients with asthma do not respond too well to this type of medication orally, a trial with several antihistaminics in turn might be worthwhile. Occasionally one is found to be particularly effective orally for a given patient. We have found them most useful, however, when given hypodermically, especially when given along with a small dose of aqueous epinephrine 1:1000. Our practice has been to administer the solution of Decapryn (2 to 5 mg.), Benadryl (5 to 10 mg.), Pyribenzamine (5 to 10 mg.) or Chlor-Trimeton (2 to 5 mg.) along with an injection of epinephrine. The antihistaminic parenterally seems to fortify and enhance the action of epinephrine and produces a more favorable effect than epinephrine alone.

Aminophylline

Aminophylline is a useful drug in asthma, but is not too effective orally in the severe attack. For this reason it is frequently given rectally in suppositories or in tap water. A child of four years or more can usually tolerate a suppository containing 0.25 gm. (3¾ grains), repeated once or twice at three to four hour intervals. For a younger child this suppository can be slit lengthwise and half the dose inserted. There are many suppositories available containing aminophylline, some with a barbiturate, others also with a local anesthetic to offset the tendency to anal irritation and burning produced by aminophylline in some patients. A number of patients exhibit toxic symptoms from aminophylline, and one should guard against overdosage with this drug. The most frequent toxic symptom in our experience is nausea and vomiting. We have seen several children with peripheral vascular collapse from overdosage. At the earliest sign of any of these adverse effects the drug should be discontinued.

Aminophylline is most effective when given intravenously. It should be given extremely slowly to avoid undesirable circulatory reactions, such as shock, rapid pulse and collapse. It is important that none be injected subcutaneously, since it causes excruciating pain when deposited under the skin. The dose intravenously is 0.006 gm. per kilogram of body weight (1/20 grain per pound). Although its use intravenously should not be limited to status asthmaticus, it should be

reserved for more severe attacks not responding to the treatment previously outlined.

Antibiotics and Chemotherapy

Antibiotics and/or chemotherapy should be administered early in the attack for associated respiratory infection if present. In our experience parenteral penicillin has been most effective in diminishing the severity of respiratory infections in asthmatic children. Penicillin sensitivity, even with repeated courses, is extremely rare in children in contradistinction to adults. Our practice has been to administer 300,000 units of procaine penicillin G intramuscularly on two to three successive days. Bicillin (Wyeth) is said to produce sustained therapeutic blood levels of penicillin for five to seven days, and it is worthwhile administering 300,000 units along with the initial dose of procaine penicillin G. This material is now available combined in one injecton. The initial dose of parenteral penicillin can be followed by penicillin orally in doses of 100,000 to 250,000 units every four hours, depending on the age of the patient. Penicillin therapy is usually enhanced by the simultaneous administration of a sulfonamide preparation. A number of oral penicillin preparations are available in tablet or liquid combined with suitable dosages of triple sulfa.

We have also used with excellent results many of the wide-spectrum antibiotics such as Terramycin, Aureomycin or erythromycin stearate. We prefer the last because of the lesser frequency of undesirable gastrointestinal side reactions and less likelihood of adverse changes of gastrointestinal bacterial flora. Ilotycin suspension (Lilly) is one of the most palatable of the erythromycin syrups available at present. The dosage of these antibiotics is 100 mg. every four hours for a child over three years and 50 mg. for a child under three years.

We have found it useful for the mother to have available oral penicillin, one of the broad-spectrum antibiotics and/or a sulfonamide preparation so that treatment can be started at the very onset of a respiratory infection. By this procedure many attacks of asthma are lessened or aborted. Only by trial and error can one determine which one of the many preparations and combinations is best for a given patient. Our practice is to continue in subsequent attacks with the one to which the patient responds best, rather than rotate through the list of antibiotics as some have recommended.

ACTH and Cortisone

The introduction of these powerful hormones has placed in the hands of the physician a potent and effective weapon for use in acute allergic

states. Treatment with corticotropin (adrenocorticotropic hormone—ACTH) and cortisone should never be undertaken lightly because of the possibility of serious side effects. Treatment with these hormones is never a substitute for thorough allergic study and search for specific etiologic factors with subsequent specific avoidance or desensitization. For this reason we limit the use of these drugs to short-term therapy of three to five days for acute asthmatic episodes when the measures already outlined have not been successful in terminating an attack. One should not wait until status asthmaticus has developed to resort to this measure. ACTH gel (HP Acthar gel, Armour, or ACTH gel, National Drug) is our treatment of choice under these conditions. There is some evidence that in the acutely ill patient a more prompt response is obtained with ACTH than with cortisone. Much less hormone is required using repository ACTH than with the aqueous solution. The slow absorption simulates physiologically the mild gradual stimulation of the adrenal cortex produced by continuous intravenous administration. One injection daily for three to five days is generally sufficient to terminate a severe attack.

The dosage of ACTH gel for a child of five years or over is as follows:

1st day	20–40 units
2nd day	20 units
3rd day	10–20 units
4th day	10 units if necessary
5th day	10 units if necessary

Below five years we have used one half to one third of this dosage, depending on the age of the child and severity of the attack. We have seen no side effects in many asthmatic children treated for only three to five days in this fashion. However, careful supervision is necessary when using these potent drugs. One must remember that resistance to infection is undoubtedly lowered by these hormones; therefore antibiotics and/or chemotherapy must be used concomitantly should an infection be present.

Many clinicians use cortisone orally instead of ACTH, but in our experience ACTH gel produces remissions faster with smaller doses. Occasionally some patients do not react to ACTH gel, probably as a result of toxic depression of the adrenal cortex, and require cortisone. We have also used cortisone in patients in whom daily injections were impossible. The dosage of cortisone in asthma is as follows, for children over five years:

1st day	25 mg. 3–4 times a day
2nd day	25 mg. twice a day
3rd day	25 mg. once or twice a day
4th day	25 mg. once a day
5th day	15 mg. once a day

Hydrocortisone acetate (Cortef, Upjohn; Cortril, Schering) is also useful. It is said to produce side effects much less frequently than cortisone. There is some evidence that it may be more physiologic than cortisone. For short-term therapy these possible advantages may not be too evident. The dosage is approximately two-thirds that of cortisone. Our experience so far is too limited to draw any conclusion as to whether hydrocortisone has any advantages over cortisone for short-term therapy (three to five days) of acute asthma. For long-term therapy its supposedly lesser tendency to produce side reactions would undoubtedly be a point in favor of its use. No data are yet available to establish a definite relationship between dosages of these hormones and body weight. The starting doses and "stepping-down" doses given are average and should vary, depending on the severity of the disease and body size.

STATUS ASTHMATICUS

When asthma continues unrelieved despite the measures already detailed, the patient is considered to be in "status asthmaticus." This is a serious medical emergency that is best treated in a hospital.

Oxygen

An oxygen tent should be ordered for severe dyspnea or rapid respiration. One should not wait in children until cyanosis occurs. The oxygen should be at room temperature. If it is cold, the cough may be aggravated. It is frequently well to admit steam to the oxygen tent to thin out and loosen the secretions. Helium-oxygen mixtures are not necessary in the treatment of asthma in children.

Hydration

At this stage in the illness there is usually considerable dehydration. Intravenous fluids should be administered in the form of 5 or 10 per cent glucose in water, in amounts of 250 to 500 cc. once or twice during the first twenty-four hours, depending on the age and weight of the child and the extent of the dehydration. Hydration is important, not only to restore body fluids, but also to assist in thinning out the bronchial secretions frequently inspissated at this stage of the attack. These children are frequently in ketogenic acidosis due to carbohydrate starvation as a result of either vomiting or low food intake.

Glucose

Glucose is advisable intravenously, not only to overcome the ketosis frequently present, but also to restore liver glycogen. This is frequently

depleted as a result of many injections of epinephrine plus failure to take or retain adequate nourishment. Depletion of liver glycogen may be a factor in the failure of epinephrine to function in status asthmaticus. One often sees epinephrine again effective after glucose intravenously. We have frequently resorted to 20 to 30 cc. of 25 or 50 per cent glucose intravenously after the initial 5 or 10 per cent intravenous infusion when we have suspected plugging of bronchi, with excellent results. This procedure apparently is effective by reducing edema of the bronchial mucosa through its osmotic action, thus releasing a bronchial plug.

Aminophylline

Aminophylline intravenously, as outlined earlier, should be continued and is conveniently given either along with the glucose infusion, or combined with 25 or 50 per cent glucose in the same syringe.

Sedation

Sedation with barbiturates should be continued, either rectally or by mouth. Again it should be emphasized that *morphine should never be used in asthma.*

Antibiotics and Chemotherapy, and ACTH and Cortisone

These should be prescribed as previously outlined.

Bronchoscopy

We have never resorted to bronchoscopy during status asthmaticus in children. However, in the presence of severe bronchial plugging this measure may be lifesaving, and one should not wait too long should it be necessary. It is our experience that with the measures outlined earlier the use of bronchoscopy for the relief of bronchial plugging should not be required often in the treatment of status asthmaticus in childhood.

REFERENCES

1. Bowen, R.: Some Practical Suggestions in the Management of Asthmatic Children. M. Rec. & Ann., 39:1189, 1945.
2. Dees, Susan C.: The Use of Aminophylline Rectal Suppositories in the Treatment of Bronchial Asthma. J. Allergy, 14:492, 1943.
3. Glaser, J.: The Symptomatic Treatment of Bronchial Asthma in Infancy and Childhood. Am. Prac., 1:4, 1946.
4. Lell, W. A.: Bronchoscopy as an Aid in the Diagnosis and Treatment of Allergic Pulmonary Disease. Arch. Otolaryngol., 43:49, 1946.

5. Levin, S. J.: ACTH in Gelatin—Clinical Results with Repository Adrenocorticotropic Hormone in Allergic Diseases. Ann. Allergy, 11:157, 1953.
6. Levin, S. J., and Moss, Selma S.: Antihistaminic Drugs—Oral, Parenteral and Topical Uses in Allergic Diseases. J. Michigan M. Soc., 49:207, 1950.
7. Levin, S. J., and Moss, Selma S.: Repository Penicillin Injections in Allergic Children. Ann. Allergy, 9:471, 1951.
8. Pratt, E. L.: Acute Bronchiolitis in Infants. M. Clin. North America, 28:1098, 1944.
9. Ratner, B.: Allergy in Childhood. V. Choice of Drugs in the Treatment of the Asthmatic Attack. New York State J. Med., 42:2029, 1942.
10. Round Table Discussion: Use of ACTH, Cortisone and Allied Substances. Pediatrics, 2:515, 1953.
11. Schick, B., and Peshkin, M. M.: Bronchial Asthma, in Brennemann's Practice of Pediatrics. Hagerstown, Md., W. F. Prior & Co., Inc., 1953, Vol. 2, Chap. 57.
12. Swineford, O., Jr.: Don't Do This for Asthma. Virginia M. Monthly, 80:129, 1953.

469 Fisher Building
Detroit 2, Michigan

VALUE OF VACCINE TREATMENT IN ALLERGIC RESPIRATORY CONDITIONS

JEAN CRUMP, M.D.

Vaccine therapy in allergic respiratory conditions is relatively difficult to discuss. Many allergists have used this procedure at some time, but their opinions as to its value are diversified. In this discussion I shall attempt to show both sides of the picture and present our own reaction to the problem.

Vaccines, filtrates, toxoids and vaccine combined with house dust have all been tried, and markedly varying results have been reported. In our hands vaccines prepared from bronchial secretion or from nose and throat cultures have proved invaluable. In the hands of another pediatric allergist, Jerome Glaser,[4] vaccine therapy has presented another picture. He says. "Frankly I am very skeptical as to the specific value of vaccine." Flensberg[3] uses vaccines, but reports that 26 per cent of his series of 162 cases showed reactions of varying severity. Berquist[1] reports that he had satisfactory results in only 56 per cent of his children. Eilerstein[2] reported a fatal case following vaccine therapy. Swineford[6] expressed his opinion as follows: "Treatment with bacterial antigen while still empirical is often but unpredictably effective."

Respiratory allergy in children presents itself in several different ways. The most common of these and certainly the type most frequently recognized is asthma. Allergic cough is often mistaken for bronchitis or is listed as a "cold." Yet when adequately studied, it may prove to be another manifestation of allergy. Nasal allergy (vasomotor rhinitis) is an important problem and one of the most difficult to treat. Hay fever, frequently termed pollinosis, is a highly specific entity and is usually readily amenable to treatment.

From the Department of Pediatrics, Woman's Medical College, and the Hospital of the Woman's Medical College, Philadelphia.

It is not the purpose of this paper to discuss respiratory allergy as a whole, but to consider treatment of given conditions by vaccine therapy.

NASAL ALLERGY

Nasal allergy plays a much more important role than often seems apparent. It is frequently seen in conjunction with asthma, but does appear as an isolated entity in many cases. Frequently children are thought to be having repeated "colds," and treatment and diagnosis are in consequence delayed. In over thirty years of work with allergic children we have seen relatively few cases of pure nasal allergy, i.e., the type frequently called "vasomotor" rhinitis. Some of the cases are definitely traceable to infection in the nose, throat or sinuses, and many require operation to remove infected tissue or facilitate drainage. Other cases, however, seem to be refractory to treatment.

Hansel,[5] discussing allergy in children, presents a table from the work of Dr. Katherine Bain, in the pediatric allergy clinic of Washington University, in which she records that in 200 children, fifty-two had nasal allergy only, forty had asthma, nasal allergy and hay fever, five had perennial nasal allergy and hay fever, and four had hay fever only.

These figures correspond with our own findings, but our percentage of so-called pure nasal allergy is considerably lower. Tuft[7] states that in his opinion "either stock or autogenous vaccine when there is definite complicating sinus infection, may be of specific value," and he has continued to hold this opinion.[8]

Vaccine therapy alone in our hands has not been particularly successful in this condition. In almost every case it has been necessary to combine other types of treatment while administering vaccine, i.e., elimination of foods or inhalants (particularly molds and environmental factors) to which the child reacts. Even with combined therapy we have not always been successful. Some allergists prefer to use stock vaccines or filtrates in the treatment of these cases, while others prefer to use an autogenous vaccine. We have tried all types, but we reiterate that our own experience has not led us to believe that vaccine therapy alone is of much value.

ALLERGIC COUGH

Allergic cough is not always easy to diagnose. Frequently this symptom complex seems to be the forerunner of true asthma, but we have seen a number of cases that do not progress beyond this point if they are treated promptly.

Only in a few cases have we felt the necessity of using vaccine therapy. Frequently these children have "colds" and show nose and throat path-

ology. Removal of foci of infection may be all that is essential to clear up the condition, but if vaccine therapy does seem indicated, we prefer an autogenous vaccine made from nose and throat cultures. At times we do use a stock vaccine, but we are more inclined to combine it with an autogenous vaccine than to use it alone.

ASTHMA

Our studies with asthma date back to the time (thirty years ago) when we were working in the allergy clinic at the University of Pennsylvania. We were greatly disturbed by the number of children who, in spite of careful study and thorough treatment with all recognized methods of therapy, continued to have severe asthma associated with every "cold." Hyposensitizing materials from nasal cultures, tonsils, sputum, house dust, and so forth, had all been tried, and the results in many

TABLE 30. *Organisms Reported in Pure Cultures*

	FIRST SERIES 112 CASES	SECOND SERIES 252 CASES
Nonhemolytic streptococcus	24	18
Streptococcus viridans	17	10
Nonhemolytic staphylococcus albus	6	4
Hemolytic staphylococcus aureus	6	4
Hemolytic staphylococcus albus	3	4
Pneumococcus	4	0
Streptococcus hemolyticus	0	2

cases were most discouraging. Roentgenograms of sinuses and chests and thorough examination by the otolaryngologist revealed variable pathologic lesions. When necessary, surgery had been tried. At this time we decided to see what results might be obtained by examining the tracheobronchial tree through the bronchoscope and by preparing a vaccine from the secretion obtained.

The results of these examinations were surprising, and after treating about 100 patients we felt that we were warranted in continuing our investigation. Continuing our studies in this line, we later read a paper covering 252 cases and 888 bronchoscopic examinations. Briefly, these cases all showed a marked inflammatory reaction in the tracheobronchial tree, some relatively mild, others severe even to the point of production of granulation tissue which bled on touch. Secretion was always obtained and almost always was reported in considerable quantity. It varied in type from mucopurulent to thick purulent material. Culture of this material frequently revealed only a single organism, which often differed from that obtained from nose and throat cultures.

As we have also reported, a series of 112 cases showed a definite pre-

dominance of streptococci. Staphylococci were frequent offenders. In many of these the organisms were reported in pure cultures. Similarly, in another report of 252 cases and 888 bronchoscopic studies the cultures revealed again a predominance of streptococci.

Results from the removal of tenacious or purulent material of bronchial secretion were almost always immediately and dramatically effective. This relief was of course only temporary.

TABLE 31. *Organisms Reported in Combination (364 Cases)*

Nonhemolytic streptococcus	106
Staphylococcus albus, nonhemolytic	86
Streptococcus viridans	72
Streptococcus, hemolytic	30
Staphylococcus aureus, nonhemolytic	28
Staphylococcus albus, hemolytic	20
Staphylococcus aureus, hemolytic	18
Pneumococcus	20
Diphtheroids	8
Influenza	10
Neisseria catarrhalis	5
Bacillus coli	2
Neisseria sicca	1
Bacillus Hofman	2

PREPARATION OF AUTOGENOUS VACCINES*

Freshly prepared ground beef heart broth is used exclusively for tubes and agar plates.

Blood and plain agar plates are used. The material, collected by swab, loop or other means, is transferred to plain agar plates and then spread by means of a bent glass rod. The rod is then carried to the blood agar plates. This serves as a method of obtaining isolated colonies and makes identification easier.

Fishings are made with a platinum rod and the use of a hand lens, and carried to broth, or slants, or both, depending on the organisms.

Since most organisms multiply at different rates, mixed cultures are never collected for preparation of vaccines.

When sputum or other material is submitted in which fungi may be suspected, a third culture is prepared, using agar or Sabouraud's medium, or both.

Broth cultures, after standing and identification, are centrifuged, the supernatant fluid is discarded, and resuspension of the growth is made in sterile normal saline solution. The cultures on agar slants are stained, and the growth is collected in sterile normal saline solution.

The tubes of concentrated growth are then stoppered (rubber) and immersed in a water bath at 60° C. for one hour. During this heating the baskets containing the tubes are tilted at frequent intervals in order that all organisms may be exposed to the heating process.

Suitable dilutions of the concentrated vaccine and sterility tests are made.

DOSAGE AND TECHNIQUE

In the early work with bronchoscopic vaccine we used two dilutions;

* Method of Dr. Claude P. Brown.

one contained 100,000 organisms per cubic centimeter and the other 100 million organisms per cubic centimeter.

Vaccine therapy was initiated with small doses, usually only 0.05 cc. subcutaneously. If any reaction occurred either locally or systemically, the vaccine was diluted more and more until the child could tolerate it without difficulty. At times only 10,000 organisms per cubic centimeter could be used. In several children it was necessary to give the material intracutaneously and to hold the dose at 0.05 cc. Dosage (given at weekly intervals) was increased slowly until 1 cc. of the weaker solution was given, and then the stronger solution was administered in a similar fashion.

In our first 112 cases eleven children had asthma after administration of vaccine, but no reaction was severe.

Our work with this type of vaccine has continued steadily, and we have now reached the point where we feel we have additional facts to offer. We are convinced that in the beginning we gave much larger doses than were necessary. For the past five years we have been testing our vaccines before administration, and we continue to dilute them until no wheal or erythema is produced by intracutaneous test and no systemic reaction appears. We then give the child (still at weekly intervals) 0.01 cc., 0.03 cc., 0.05 cc. and then 0.1 cc.; only rarely do we increase our dosage beyond 0.1 cc. With this method of therapy we obtain equally good results as we did with the large dosage previously mentioned, and we have not had any local or systemic reactions.

When we first proposed this type of therapy, bronchoscopists who would undertake this type of work were available in only a few cities. Now it can be carried out in a great many localities, and other observers are reporting good results from this method of therapy. (This type of treatment produces excellent results in children, but is not equally successful with adults, and the bronchoscopic findings in adults were quite different from those in children.)

We continue to use vaccine made from sinus washings, tonsils or nose and throat secretions. We have the vaccine prepared in a similar fashion as that just described, and administered in the same way, for some parents at the onset of treatment refuse bronchoscopy. We have also tried filtrates and stock vaccines, but have concluded that the results obtained from these methods are not at all comparable to results achieved with bronchoscopic vaccine. Frequently, after a year's trial with the former type of vaccine, the recalcitrant parents ask to have their child bronchoscoped.

In our experience it is of paramount importance that vaccine therapy be continued over a long time. We continue to administer it at weekly intervals until the child has been symptom-free for at least a year. Then for six months it is given every two weeks, and later every three weeks.

It is not uncommon to have a child (referred by another physician) appear for treatment who has had asthma for six to eight years. The child obtains prompt relief from bronchoscopic drainage and is referred back to the family physician for his injections. Frequently he has no asthma at all, and the family discontinue treatment after eight to nine months. Almost without exception this child will have a relapse during the next few months, and treatment will have to be given all over again.

When the child has both asthma and hay fever and the asthma has proved to be due in part to pollen, we have obtained our best results with perennial therapy. The vaccine is given weekly, and after the pollen dosage has reached the decided maintenance level, it is administered only every two to three weeks.

It is worthy of comment that since the introduction of antibiotics and chemotherapeuthic agents we do not often see children who have not had several courses of treatment with one or several of these agents before reporting to us. These drugs have changed to a considerable extent the picture in the tracheobronchial tree. Frequently little pus or mucopus is seen on examination, and the mucous membrane more nearly resembles that seen in adults. However, even though it is sometimes necessary to instill saline solution in order to wash out a little secretion, bacteria may be grown from this type of specimen, and the vaccine made from this material is just as effective as that obtained when we were observing the picture of acute infection previously reported.

The vaccine, as Dr. Brown has indicated, is made in two dilutions. The weaker solution is diluted to the concentration the child can tolerate. It is used for one year; then the concentrate is checked and diluted to the previous concentration.

In relatively few cases only does a child require more than one bronchoscopic drainage. If it seems advisable to continue vaccine after the original bronchoscopic vaccine has been "outdated," then a stock vaccine or toxoid can be used satisfactorily for one year or more. It is perhaps pertinent to add that we use a tuberculin syringe for measuring all our doses.

There are few available statistical data on the use of vaccine therapy in the allergic child. Different types of vaccines and different techniques in the hands of many allergists apparently give variable results.

CONCLUSIONS

After thirty years work with allergic children and study of more than 1500 bronchoscopies, our conclusion at this date can be stated succinctly: i.e., in our hands the use of bronchoscopic vaccine in asthma in children is the sine qua non of therapy. The results of vaccine therapy

in vasomotor rhinitis and allergic cough are too variable for any definite conclusion to be drawn from them.

REFERENCES

1. Berquist, G.: Analysis of a Series of Asthma Cases Treated with Autovaccine. Acta med. Scandinav., *144*:2, 101, 1952.
2. Eilersten, E.: Bronchial Asthma: Present Status in Denmark and Sweden. Tidsskr. f. d. norske lægefor., 72:132, 1952.
3. Flensberg, E. W.: Universal Reactions in Treatment with Bacterial Vaccines. Acta pædiat., 39:192, 1950.
4. Glaser, J.: Personal communication.
5. Hansel, F. K.: Clinical Allergy. St. Louis, C. V. Mosby Company, 1953.
6. Swineford, O., Jr.: Bacterial Allergy. Virginia M. Monthly, 80:417, 1953.
7. Tuft, L.: Clinical Allergy. Philadelphia, W. B. Saunders Company, 1937, p. 366.
8. Tuft, L.: Clinical Allergy. 2d ed. Philadelphia, Lea & Febiger, 1949, p. 104.

906–7 Aldine Building
Philadelphia 3, Pa.

GASTROINTESTINAL MANIFESTATIONS OF ALLERGY IN CHILDREN

JOSEPH H. FRIES, M.D.

It is strange that a clinical entity so specifically named as "gastrointestinal allergy" should be so often confused. Properly analyzed, gastrointestinal allergy must be an allergic response and must occur in the gastrointestinal tract. It is a consequence of union of antigen with the specific reagin (antibody) residing in the tissues of the alimentary tract. It not only can be a specifically localized tissue response, but may be part of a more widespread reaction with other shock organs participating. In contrast, it should be obvious that "food allergy" implies the simple and specific concept of allergy to foods. Such hypersensitiveness is capable of provoking symptoms in any tissue of the body, including the gastrointestinal tract. Both terms are frequently interchanged.

Today the term "gastrointestinal allergy" unfortunately is loosely used to cover obscure digestive disorders which actually are organic or psychic, or, conversely, complaints due to food sensitivity, wherein the gastrointestinal tract is not even the shock or reactive organ.

INCIDENCE

The incidence of gastrointestinal allergy does not lend itself to statistical determination. Inasmuch as the diagnosis is being used with increasing frequency as a label, especially in obscure, vague and indefinite disturbances of the digestive tract, accurate diagnoses of gastrointestinal allergy are few in number. Mild episodes are difficult to substantiate. Those which are immediate, severe and consistently and repeatedly provoked are easier to recognize.

The incidence of gastrointestinal allergy is not static, inasmuch as it decreases with increase in age. Early literature on allergy mentions

the transition of infantile eczema to asthma, and of "abdominal migraine" to a cephalic type.[1] The spontaneous shift of reactivity, with increase of age, from the gastrointestinal tract (as from the skin) to other organs would result in a larger incidence of this malady in infants, in contrast with the older child or adult. Certain physiologic and anatomic changes occur in the skin which make it less vulnerable in later years, and by analogy it may be reasoned that comparable alterations occur in the gastrointestinal tract. Sensitivity to food, which is the most common cause of allergic reactions in the digestive tract, is also more frequently encountered in infancy and gradually and spontaneously decreases with maturity. For these reasons no definitive statistics of incidence are available.

MECHANISM

The mechanism by which the allergen is brought into contact with the sensitized cells, thereby provoking gastrointestinal symptoms, may be that of direct or indirect exposure. The allergic reaction resulting from direct contact of the causative substance, usually a food, with the mucous membrane lining of the digestive tract is usually immediate. This is probably the phenomenon which produces the sudden swelling and blistering of the buccal mucosa, or the nausea and vomiting which may ensue immediately after ingestion.

A further demonstration of reaction resulting from direct mucosal contact was the experimental production of colonic spasm promptly on the rectal instillation of an allergen in a barium enema in specifically sensitive subjects. The spasm which was demonstrable roentgenographically was not seen with a plain barium enema.[6, 7] Secondly, production of gastrointestinal disturbances may involve the absorption of the antigen into the blood stream and its return via the circulatory system to the specifically reactive portion of the digestive tract.[21] This would account for allergic reactions in the lower bowel (e.g., rectal tenesmus) immediately after ingestion.

Remarkably illustrative are the allergic reactions which have been induced experimentally in the exposed digestive tracts of passively sensitized rhesus monkeys and of human beings.[22, 23] The clinical reaction, whether immediate or delayed, consists in mucosal edema, hyperemia and concomitant hyperactivity of the secretory and mucous glands, with secondary muscle spasm.

ETIOLOGY

Gastrointestinal reactions are most commonly caused by foods. In order of decreasing frequency of incrimination, they are milk, egg,

chocolate, fish, nuts and orange, in addition to almost any other food. Drugs such as acetylsalicylic acid, sulfonamides, antibiotics and vitamins are occasional offenders. Parenterally injected substances such as pollen extracts and antibiotics may cause systemic allergic reactions in which the digestive tract participates; on rare occasions the digestive tract may be the only shock organ. Still more infrequent are gastrointestinal reactions to inhalants (osmyls), and these do not constitute a problem in the average pediatric practice.

SYMPTOMATOLOGY

There is no symptom or pattern of symptoms which is specifically characteristic for allergy per se. Moreover, a single symptom (allergic abdominal pain, for example) may vary in its intensity, reaction time, duration, constancy, and association with coexisting symptoms. It helps to group these varied clinical manifestations according to the portion of the gastrointestinal tract involved, as follows:

Buccal and pharyngeal
Gastric
Intestinal
Miscellaneous (e.g., constitutional reactions in which the gastrointestinal tract participates, mucous colitis,[11] rectal bleeding[17])

Visible changes of the digestive tract are readily recognized, such as angioedema of the buccal mucous membrane, palate, pharynx and tongue. Changes of the stomach and intestines are not normally visible. However, one must appreciate that these changes can and do occur in these less observable organs.[14] Symptoms of urticaria or angioedema of the skin or mucous membranes concomitant with alimentary disturbances imply that similar changes may be occurring in these less obvious parts of the gastrointestinal tract.

Groups of symptoms may form patterns not commonly characteristic of disorders on a hypersensitive basis. Some of these syndromes, heretofore considered organic and functional, are now recognized as being provoked on occasion by an allergic reaction, among them recurrent vomiting, pylorospasm, the celiac syndrome and colitis.

Protective Mechanisms

The body utilizes several mechanisms to protect itself from encounters with substances noxious to the host. With reference to ingestants, these "protective" mechanisms vary from rejection to rapid expulsion of the substance from the bowel. For example, there is frequently a pronounced dislike for a specific allergenic ingestant when the untoward response is in the gastrointestinal tract. In infants a previous

experience or two with a burning taste in the mouth or other unpleasant sensation implants a memorable impression resulting in subsequent refusal of the food. If the food is accepted into the mouth, the child may reject it by spitting it out after the food has made contact with the buccal mucosa. In our experimental studies of ingestion of allergens[6, 7] there was sometimes difficulty in getting children to swallow the antigen even when disguised in a barium meal.

Nausea is most frequent in severe immediate types of gastrointestinal allergy to foods.[8] Vomiting is also common in severe sensitivity and represents a method of getting rid of the food substance before it is passed on to the intestine.[8]

Pylorospasm, by meting out small portions either through a narrowed obstructed pylorus or through prolonged, intermittent closures, slows down the rate of delivery of the antigen to the mucosal surfaces of the intestine.[3]

Esophagospasm and cardiospasm are observable, although rare, "protests" to the passage of an antigen into areas of greater absorption.

Diarrhea is a common method by which the host disposes of the antigen as rapidly as possible, thereby minimizing absorption.

One can deduce that the forcing or disguising by parents of a specifically disliked or rejected food, especially one not essential to nutrition, is unwise and probably contrary to nature's intention in a known allergic child. Furthermore, it can be questioned whether a food which is producing physiologic disturbances in the gastrointestinal tract is adequately utilized nutritionally.

Abdominal Pain

The classification of allergic abdominal pain made by the author[5] in 1936 is still serviceable, utilizing three arbitrary divisions, depending on severity:

1. Severe abdominal pain, simulating an acute surgical condition of the abdomen in which differentiation from appendicitis, gallbladder disease, and so forth, is challenging
2. Abdominal pain of subacute recurrent nature
3. Abdominal pain as a subsidiary symptom (appearing during acute attacks of asthma or, more often, during severe outbreaks of urticaria or angioneurotic edema).

Recurrent Vomiting

Vomiting (recurrent, cyclic or periodic) is a symptom-complex due to a variety of causes, including food hypersensitiveness. Studies by the

writer[4] on selected allergic children noted that the purposeful ingestion of an offending food initiated attacks of vomiting, sometimes prolonged or recurrent. The avoidance of this food resulted in comparative freedom from attacks. Clinical sensitivity to a specific food correlated with positive cutaneous tests and passive transfer tests.

There are many variables which make the establishment of proof in suspected cases difficult. There are "anergic" periods and changes in the threshhold of tolerance depending on precipitating factors of stress, infection, and the like. Furthermore, there is the possibility of cumulative effects from the ingestion of the same allergen or a combination of different allergens.

Pylorospasm

Visualization of allergic manifestations in the gastrointestinal tract by fluoroscopy and roentgenogram has made it apparent that the pylorus plays a large role in the allergic symptomatology of the stomach, a variety of disturbances of the pylorus being observed. Roentgen changes and associated gastrointestinal symptoms are reproducible experimentally by intentional feeding of barium meals containing the allergen.[3] Such experiments point out that in the clinical interpretation of abnormalities in the pylorus the possibility of allergic involvement must be considered. In the opinion of some authors, constantly recurrent spasm of the pylorus may result in muscular hypertrophy, which may in some instances lead to pyloric stenosis.[12]

NUTRITION

Nutritional impairment in children with chronic, recurrent gastrointestinal reactions—as with other gastrointestinal disorders—is to be expected. Clinically, one sees, in severe instances, skin lesions which are highly suggestive of vitamin A deficiencies and evidences of other vitamin deprivations. Growth is sometimes stunted, and there may be impairment of musculature.

The refusal of various foods frequently encountered results in a poor, finical eater, the child subconsciously associating nausea and other unpleasant reactions with intake of food. Severe restrictions in diet of essential foods such as milk, eggs, legumes, readily embarked upon by enthusiastic physicians, cause havoc if followed too long or compensated for inadequately. Incomplete utilization of nutrients and vitamins resulting from disturbed motor function of the digestive tract certainly must exist. In addition, local angioedema may be induced which may affect the permeability of the gut for the ready passage of

nutrients. In support of this, in studies as yet incomplete, I have observed interference with the absorption of vitamin A as indicated by an abnormally flat absorption curve in a few children with severe gastrointestinal allergy.

DIAGNOSIS

The capriciousness of gastrointestinal allergy makes it necessary that all possible organic and psychic factors be thoroughly explored. It is worthy of repetition that allergy accounts for only a small percentage of digestive disorders in children.

History

A careful history is of primary importance. It is in this field that a leisurely and detailed questioning of the parents (and, when possible, the patient) can be most informative. Cognizance should be taken of any possible association which may have been made between ingestants and symptoms, of food dislikes, and of common allergenic foods being eaten in large amounts. A familial or personal background for allergy, or association of other allergic manifestations in other shock tissues, gives confirmation that the gastrointestinal symptoms may be on an allergic basis.

Cutaneous Tests

The frequent failure of cutaneous tests to correlate positively with proved clinical digestive symptoms of food hypersensitiveness points to the limitation of this diagnostic procedure. Occasionally, however, cutaneous reactions of the immediate wheal type do indicate the offending antigen. These range from markedly positive to negative reactions, both by direct and passive transfer methods. It is noteworthy that those patients demonstrating immediate, pronounced gastrointestinal disturbances are the ones who most frequently give marked positive dermal reactions (Table 32).

Positive cutaneous reactions sometimes are obtainable with higher concentrations of the testing extracts, although not with the routine testing strengths. Sensitization may possibly exist specifically to the digested products of foods—to the proteose or other split derivatives of proteins, and not to the natural food.[2, 19] In such cases routine cutaneous tests are negative. The absence of reactions in some subjects possibly may be due to the existence of other forms of food intolerance which are not based on a reaginic mechanism.

TABLE 32. *Skin Reactions Resulting from Intracutaneous Testing of 30 Children with Gastrointestinal Allergy*

ALLERGEN	NITROGEN CONTENT IN MG. PER CC., OR DILUTION	DEGREE OF REACTION	AGE OF PATIENT IN YEARS
Egg	0.0001	++++ (x)*	3
Egg	0.0001	++++ (x)	6
Egg	0.0001	++++ (x)	6
Egg	0.0001	+++ (x)	6
Egg	0.01	+++	8
Egg	0.01	+++	7
Egg	0.01	++	5
Egg	0.01	++	12
Egg	0.01	+	7
Egg	0.01	+	8
Egg	0.01	+	12
Egg	0.01	0	12
Egg	0.01	0	6
Egg	0.01	0	5
Egg	0.01	0	11
Egg	0.01	0	9
Codfish	0.00001	++++ (x)	6
Codfish	0.00001	++++ (x)	10
Herring	0.0001	+++	13
Walnut	0.005	++++ (x)	6
Almond	0.05	+++	11
Almond	0.05	+	14

* (x) indicates patients who had marked clinical disturbances following ingestion of the allergenic food.

The technique used consisted in the intracutaneous injection of about 0.02 cc. of the testing extract. Reactions were classified according to the size of the wheal.

TABLE 32 (*Continued*)

ALLERGEN	NITROGEN CONTENT IN MG. PER CC., OR DILUTION	DEGREE OF REACTION	AGE OF PATIENT IN YEARS
Wheat	0.05	++	4
Wheat	0.05	+++	8
Cabbage	1:5	++++ (x)	7
Sweet corn	1:5	+++	12
Oats	1:10	+	10
Milk	1:10	0	5
Milk	1:10	0	7
Milk	1:10	0	9

Roentgen Findings

Intentional feeding of an identified allergenic substance for the purpose of inducing roentgenographic changes and the use of a contrasting meal of plain barium were reported first by Serio[18] and later Rowe.[16] These reports were followed by the writer's studies on children,[6, 7] which have since been corroborated by other workers.[13, 20]

In my studies, gastric retention, hypermotility and gastric atony have been visualized in children (Fig. 33). Alterations in the roentgenographic pattern of the small intestine were infrequent. However, some instances of segmentation and hypermotility were observed. Regional constriction or dilatation of the large bowel also occurred occasionally. Furthermore, I have demonstrated marked spasticity of the transverse and descending colons by means of barium enemas containing antigen.

Although the alterations found in the allergic gut are not pathognomonic, their presence should suggest the possibility of allergic gastrointestinal disturbances, particularly when other confirmatory findings are present.

Food Diary

For lack of accuracy of the skin test and of all other finite tests, reliance must be placed on a detailed food diary and on controlled ingestion trials of suspect foods. The food diary must record daily intake

of all possible ingestants, including vitamins, medications and between-meal "snacks," in the quantity ingested and indicating time relationships. This should be paralleled by a record of symptoms in their proper time relationship.

Trial Ingestion

With the clues provided by the history and by the food diary, ingestion of the suspected foods should be tried under controlled circumstances. Only one food may be tested at a time. This test should be

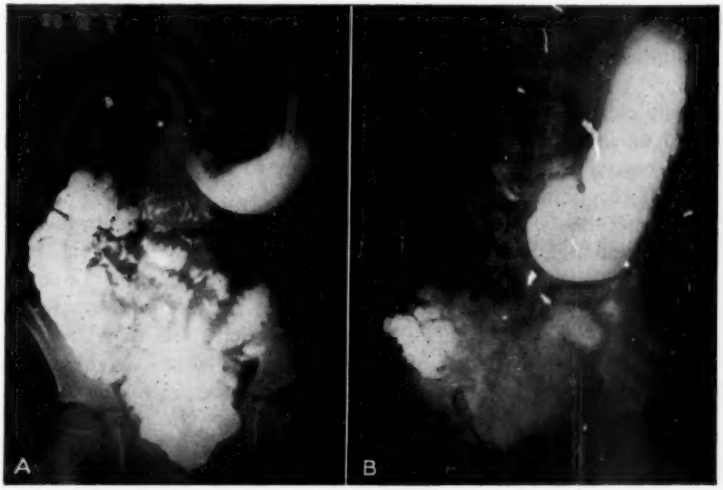

Fig. 33. Roentgenograms of a 6 year old boy who had asthma. Ingestion of nuts on many occasions caused vomiting and abdominal pain. Skin tests (intracutaneous) to almond, walnut and Brazil nut were positive.

The roentgenograms shown here were 6 hour studies. *A*, Control with plain barium sulfate shows slight retention within the stomach. *B*, A comparative study with ½ teaspoonful of nut added to the plain barium, without the patient's knowledge, shows gastric retention of more than two thirds of the meal. There is also marked spasm (closure) of the pylorus.

made on an empty stomach, preferably in the morning, and when the child is symptom-free. A small amount of the test food is given, and after fifteen to thirty minutes an increased quantity of the food is fed until symptoms are provoked or until the amount ingested considerably exceeds the quantity customarily eaten. When disturbances are delayed and occur beyond the testing period, the trial must be repeated for confirmation.

Laboratory Investigations

Determination of the eosinophil content of the blood is of questionable value because it varies widely from day to day. The leukopenic index[9] has proved equally unreliable in my experience.

Rectal smears for eosinophils I have tried sporadically with questionable success and feel that further observation should be made before evaluating the favorable conclusions of others.[15] One must bear in mind that destructive processes in the colonic area, or parasitic infestations, are also capable of producing eosinophils in the mucus obtained from the rectum.[24]

TREATMENT

Elimination of food or chemical offenders is, of course, ideal therapy. In some instances, however, trial diets and cutaneous tests still fail to identify clearly all the incitants. In this circumstance the child can be placed on an empirically determined hypoallergenic diet, not ignoring the necessary inclusion of substitute foods to meet vitamin and nutritional requirements.

This diet makes liberal use of foods processed by heat or dehydration, which lower their allergenicity (evaporated milk, dehydrated banana), and of foods of known low allergenicity even when these may be somewhat unusual in a child's diet (beet tops, Swiss chard, soy beans).

When symptoms are controlled by such a diet, foods may be added gradually, paying particular attention to the detection of any which may cause untoward reactions.

Hyposensitization by injection of an extract of the offending food is not only hazardous, but has never proved effective; nor has oral desensitization been successful in my experience.

The antihistaminic drugs have been of doubtful value. I have had no experience with the use of corticosteroids for this type of allergic reaction, but presume that they might be effective for a severe episode when other agents have failed.

Since most allergic gastrointestinal symptoms decrease with increasing age, the duration of the necessity for limitation of foods and of supportive medication should be relatively short.

Whether it will ever be possible completely to prevent development of allergic reactions in the gastrointestinal tract is questionable, on the basis of the knowledge of immunology we have to date. It would seem, however, that active sensitization of the digestive tract in children of known allergic inheritance might be minimized by the avoidance in early years of the more common, potent antigenic ingestants. A long-term study in this direction has been reported by Glaser and Johnstone.[10]

REFERENCES

1. Bray, G. W.: Recent Advances in Allergy. 2d ed. Philadelphia, P. Blakiston's Son & Co., 1934, p. 370.
2. Cooke, R. A.: Protein Derivatives as Factors in Allergy. Ann. Int. Med., *16*:71, 1942.
3. Fries, J. H.: Roentgen Studies of Allergic Children with Disturbances of the Pylorus Resulting from Food Sensitivity. J. Allergy, *23*:39, 1952.
4. Fries, J. H., and Jennings, K. G.: Recurrent Vomiting in Children. J. Pediat., *17*:458, 1940.
5. Fries, J. H., and Merrill, G. A.: Allergic Abdominal Pain in Children. Am. J. Dis. Child., *52*:1107, 1936.
6. Fries, J. H., and Mogil, M.: Roentgen Observations on Children with Gastro-intestinal Allergy to Foods. J. Allergy, *14*:310, 1943.
7. Fries, J. H., and Zizmor, J.: Roentgen Studies of Children with Alimentary Disturbances Due to Food Allergy. Am. J. Dis. Child., *54*:1239, 1937.
8. Fries, J. H,. and Zizmor, J.: Gastrointestinal Allergy in Children. J. Pediat., *16*: 69, 1940.
9. Gay, L. P.: Gastro-intestinal Allergy. IV. The Leukopenic Index as a Method of Specific Diagnosis of Allergy Causing Peptic Ulcer. J.A.M.A., *106*:969, 1936.
10. Glaser, J., and Johnstone, D. E.: Prophylaxis of Allergic Disease in the Newborn. J.A.M.A., *153*:620, 1953.
11. Hollander, E.: Mucous Colitis Due to Food Allergy. Am. J. M. Sc., *174*:495, 1927.
12. Horowitz, A., Alvarez, W. C., and Ascanio, H.: The Normal Thickness of the Pyloric Muscle and the Influence on It of Ulcer, Gastroenterostomy and Carcinoma. Ann. Surg., *89*:521, 1929.
13. Lepore, M. J., Collins, L. C., and Sherman, W. B.: Small Intestine Roentgen Studies in Food Allergy. J. Allergy, *22*:146, 1951.
14. Pollard, H. M., and Stuart, G. J.: Experimental Reproduction of Gastric Allergy in Human Beings with Controlled Observations on the Mucosa. J. Allergy, *13*:467, 1942.
15. Rosenblum, A. H., and Rosenblum, P.: Gastrointestinal Allergy in Infancy. Pediatrics, *9*:311, 1952.
16. Rowe, A. H.: Roentgen Studies of Patients with Gastrointestinal Food Allergy. J.A.M.A., *100*:394, 1933.
17. Rubin, M. I.: Allergic Intestinal Bleeding in the Newborn: Clinical Syndrome. Am. J. M. Sc., *200*:385, 1940.
18. Serio, F.: La sintolmatologia radiologica della anafilassi gastro-intestinale. Riforma med., *48*:1742, 1932.
19. Stull, A. H., and Hampton, S. F.: The Study of Antigenicity of Proteoses. J. Immunol., *41*:143, 1941.
20. Tallant, E. J., O'Neill, H. A., Urbach, F., and Price, A. H.: Gastro-intestinal Food Hypersensitivity: Roentgen Demonstration. Am. J. Digest. Dis., *16*:140, 1949.
21. Walzer, M.: Studies in Absorption of Undigested Protein in Human Beings. J. Immunol., *14*:143, 1927.
22. Walzer, M.: Allergy of the Abdominal Organs. J. Lab. & Clin. Med., *26*:1867, 1941.
23. Walzer, M., Gray, I., Strauss, H. W., and Livingston, S.: Studies in Experimental Hypersensitiveness in the Rhesus Monkey. IV. The Allergic Reaction in Passively Locally Sensitized Abdominal Organs. J. Immunol., *34*:91, 1938.
24. Withers, O. R.: Gastrointestinal Allergy. Ann. Allergy, *11*:637, 1953.

52 Eighth Avenue
Brooklyn 17, N.Y.

THE ALLERGIC CELIAC SYNDROME

DOUGLAS E. JOHNSTONE, M.D.

The history of progress in the proper labeling of children exhibiting symptoms of "celiac disease" has somewhat paralleled what has happened in the field of congenital heart disease. For years a child was thought to have "idiopathic celiac disease" if he exhibited some or most of the following symptoms: (1) varying degrees of diarrhea with bulky, mushy, fatty or foamy feces; (2) abdominal distention; (3) failure to thrive; (4) poor muscle tone; (5) recurrent infections of the upper or lower respiratory tract which might aggravate the other findings.

NEWER CONCEPTS OF THE CELIAC SYNDROME

In 1938, with the classical investigations of Dorothy Andersen, there began a new era in the history of this condition during which attempts were made to assign more specific diagnoses to some of the children having these symptoms. Andersen first pointed the way to separate from infants with this vague syndrome a group of children with cystic fibrosis of the pancreas,[1] and still later she defined those groups we now call infantile steatorrhea and starch intolerance.[4] Although there is still some doubt as to its existence as an entity, a fourth subgroup, called "incomplete pancreatic deficiency," was first described by Gordon Gibbs[7] in 1950. A still further possible entity to be differentiated from this hitherto hodgepodge group was suggested by the recent report of Lowe and May,[14] who reported two children with pancreatic trypsin deficiency, but with normal amylase or lipase. These children, unlike

From the Department of Pediatrics, University of Rochester School of Medicine and Dentistry, the Pediatric Service of the Genesee Hospital and the Allergy Clinic of the Strong Memorial Hospital, Rochester, N. Y.

those with what Andersen calls "cystic fibrosis of the pancreas," presumably have no respiratory symptoms and might not have the same fatal prognosis. Finally, the reports of Riley,[25] Kunstadter[12] and McKhann[18] have suggested with varying degrees of clarity and documentary support that we should also separate off as an additional entity the allergic celiac syndrome. It should be emphasized that by so doing it is not implied that allergy may play a role in all cases of "idiopathic celiac disease." The purpose of this paper is merely to suggest that *some* children's celiac symptoms may be on an allergic basis. It is hoped that the possibility of allergy will be considered in those cases of this syndrome in which other specific diagnostic labels cannot be made to fit the clinical facts.

DIAGNOSIS

To justify labeling a particular group of symptoms in a particular child as an "allergic celiac syndrome," certain postulates ought ideally to be met: namely, (*a*) the child should have to some degree most of the symptoms listed earlier which pediatric parlance lumps under the heading of "celiac symptoms," and (*b*) one should be able to identify, at least indirectly, an allergic process with the given set of symptoms. Unfortunately, many obscure diarrheas and intestinal disorders are labeled "allergic" with little evidence to support such a label. Such flimsy diagnoses merely provide further ammunition for those who are skeptical that this or any other clinical entity can have an allergic basis.

Before enumerating the specific criteria by which such a diagnosis can be made, an illustrative case history of a child believed to have had an allergic celiac syndrome will be presented briefly.

CASE HISTORY. K.K. appeared to be a normal infant at birth. His family history was of interest in that his mother had marked dermatographia and perennial allergic rhinitis, his father had perennial allergic rhinitis, and his paternal first cousins both had marked intolerance to cow's milk. In addition, one of these cousins now has pollinosis.

At approximately 3 weeks of age K.K. had increasingly severe postprandial "colic." By a month of age he was "screaming with belly pain" from dawn till midnight. His symptoms were labeled "colic," which was thought to be the result of parental anxiety, excessive hunger or air swallowing. Consequently, a wheat-containing cereal was added to his formula on his pediatrician's advice at approximately 5 weeks of age. Not only did this dietary addition fail to help the "colic," but the infant began to have diarrhea, passing ten or more stools daily. These were described by the patient's mother variously as "mushy, foamy, greasy, occasionally green, and always with a lot of mucus." He vomited intermittently, became irritable and had a clear mucous rhinorrhea. His abdomen became increasingly distended. Various dietary changes in the next 6 weeks (during which time the wheat was continued in the formula) failed to bring improvement in either the "colic" or diarrhea. The infant became increasingly irritable and pale, with flabby musculature, and failed to thrive.

At this point he was brought to an allergist who capitulated to the parents' entreaty to hospitalize the infant for study. In the hospital he was put temporarily on a

stock evaporated cow's milk formula. An analysis of a 3 day stool collection revealed that 47 per cent of the dried fecal weight was fat (normal for this diet was under 28 per cent). Repeated smears of strands of fecal mucus when stained with Wright's stain revealed clumps of eosinophils. A roentgenogram of his upper small intestine revealed the classical "clumping phenomenon" seen in many types of celiac disorders.[15] A glucose tolerance test resulted in a somewhat flattened curve. Vitamin A absorption tests, using both the alcohol and ester forms, were done according to the technique of Katsampes and McCoord.[17] When the test was done, using the ester form of Vitamin A, a flat curve resulted, revealing poor absorption of this form. When the test was repeated, using the alcohol form, normal absorption figures were obtained. Since these findings have been reported only for children with cystic fibrosis of the pancreas, a fatal disease, the vitamin A ester absorption test was repeated. The results of the second test roughly paralleled those of the first test. A test for fecal trypsin,[8] however, revealed that the feces contained normal amounts of tryptic activity in high dilution. To verify this finding a duodenal aspiration was performed. Examination of the pancreatic juice thus obtained revealed a high normal value for trypsin concentration, as well as that of lipase and amylase. A nasal smear revealed many clumps of eosinophils, suggesting the additional diagnosis of allergic rhinitis.

The patient was discharged on a diet of rice cereal, strained apple sauce, pears, peas, carrots, a water-soluble mixture of synthetic vitamins and a Nutramigen formula. An evaporated milk formula was finally successfully reinstituted at the age of 9 months. Wheat and eggs have been withheld from his diet until the present. He remained essentially free of symptoms until approximately 6½ months of age, when he again had bulky, loose, greasy stools. His mother suspected that squash was responsible for this upset. The symptoms disappeared when squash was discontinued and reappeared when it was reintroduced into his diet. A vitamin A ester absorption test performed 2 months later revealed normal absorption of this material compared to the original study at the time of his hospitalization.

At the time of this writing he is 21 months old and is free of symptoms. Intradermal tests to wheat, soy bean, peanut, lactalbumin and whole cow's milk, performed at 20 months of age, revealed a positive reaction to wheat, a questionable reaction to whole cow's milk, and negative reactions to soy bean, lactalbumin and peanut.

Clinical Criteria

Onset of Diarrhea after the Introduction of a New Food. The symptoms may either begin approximately three weeks after the introduction of the offending food or may occur immediately after its introduction. The latter possibility may possibly be explained on the basis of active sensitization of the infant to the food while in utero.[24] The commonest incriminated allergens seem to be wheat, cow's milk, egg and occasionally a vegetable like squash.

Improvement after Withdrawal of the Suspected Offending Food. This finding alone offers only suggestive and indirect proof of the allergic etiology of the symptoms in question, since, when milk is shown to be the offender, improvement after its withdrawal may merely indicate intolerance to cream and fat in general. This possibility, however, may be excluded if withdrawal of whole milk brings improvement and subsequent feeding of a skimmed milk formula causes a recurrence of symptoms.

Family History of Atopic Disease. Most allergists feel that the chances

of an infant exhibiting some atopic symptom are far greater if his parents and/or siblings have had some major allergy, in spite of Ratner's[23] excellent and challenging recent work which holds that "no genetic hypothesis (of allergic inheritance) can be made to fit the existing data."

Presence, History or Subsequent Development of Other Atopic Disorders in the Patient. The patient whose history has been presented had a concomitant allergic rhinitis. If a child with a celiac syndrome coincidentally acquires atopic dermatitis or asthma, the possibility that his gastrointestinal upset may be on a food allergy basis has to be considered.

Reproducibility of the Syndrome. Since the patient's diarrhea can be presumably helped by the discontinuance of an offending allergen, it should be possible to reproduce the syndrome at will by merely reintroducing the offending allergen into the diet. There is, however, some time limitation on this possibility, since most of these children develop a tolerance for the offending food in six to twelve months. On the other hand, if the child's symptoms are sufficiently distressing, one may think better than to risk restarting the patient's illness merely to satisfy these postulates. In the case reported the symptoms were accidentally reproduced by the development of clinical sensitivity to a new vegetable introduced into his diet.

Laboratory Criteria

Steatorrhea. The preferred method of demonstrating the presence of excess fecal fat is by doing a strict fat balance study. Practically, however, if an infant is placed on a diet consisting solely of whole cow's milk for three days, during which time the entire fecal output is collected and analyzed for its fat content, this should give the information needed. Normally the fat content of feces should not exceed 28 to 33 per cent of its dry weight. McCoord[16] feels that under these circumstances a child should not pass in excess of 3 gm. of fat in his feces per twenty-four hours.

Stool Eosinophilia. Unless the smears are made properly, one might easily miss the presence of significant numbers of eosinophils in fecal mucus. The key to successful demonstration of fecal eosinophilia is to collect two or three diapersful of recently passed feces and then search through the specimens with an applicator stick for strands of mucus. If one simply makes a smear of feces without including a globule of mucus, there is little hope of finding eosinophils.[20] The fecal mucus should be spread thinly on a clean slide and allowed to dry without heating.[26] The smear may then be stained with either Wright's or Hansel's stain.

Vitamin A Absorption. Normally, infants have a fasting vitamin A blood concentration of 15 to 40 McCoord units per 100 ml. of serum (1 McCoord unit equals 3.8 international or U.S.P. units). After oral administration of 7000 international units of vitamin A (either form) per kilogram of body weight, there is normally a rise of serum vitamin A concentration to 100 to 250 McCoord units. Children with idiopathic celiac disease cannot absorb *either* form of vitamin A normally, so that after the test dose of 7000 international units per kilogram of body weight is given the serum vitamin A concentration rarely rises above 50

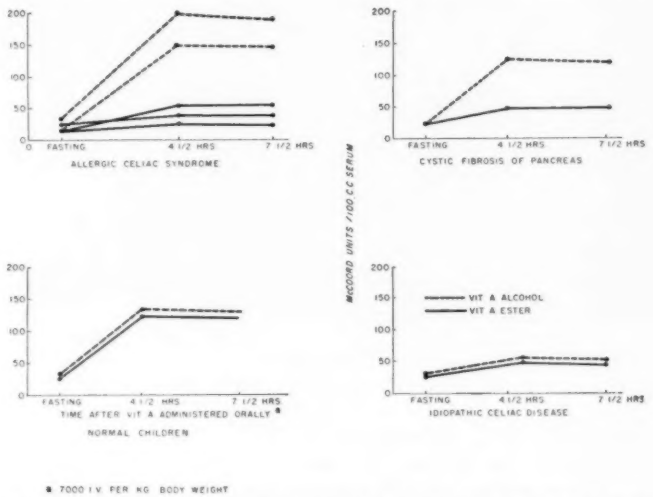

Fig. 34. Differential absorption of vitamin A ester and alcohol in children with celiac disease, cystic fibrosis of the pancreas and allergic celiac syndrome compared to normals.

McCoord units per 100 ml. of serum. Infants with cystic fibrosis of the pancreas, because their nutritional difficulties stem more from defective breakdown of fats into their basic fatty acids than from defect of absorption of normal breakdown products of fat digestion, have normal absorption of the alcohol and aldehyde forms of vitamin A. However, they fail to absorb the ester form of vitamin A (Fig. 34). Vitamin A absorption studies on four infants with allergic steatorrhea[9, 10] so closely paralleled the results found in children with cystic fibrosis of the pancreas that it was not until some of the tests had been repeated and then confirmatory normal duodenal juice enzyme concentrations had been found, that this new finding was fully appreciated.

Roentgenogram Studies of the Small Intestine. At the time a child is suffering from an allergic steatorrhea a roentgenogram of the small

intestines after swallowing barium usually reveals a characteristic clumping of the barium (Fig. 35) instead of the normal feathery pattern. This finding, however, is seen in other conditions such as cystic fibrosis of the pancreas, sprue and malnutrition. The keen observations of Fries,[6] who demonstrated gastric retention and other intestinal motility abnormalities when offending allergens are added to the barium meal, have added greatly to our knowledge of the effect of offending foods on the intestinal tract of these infants.

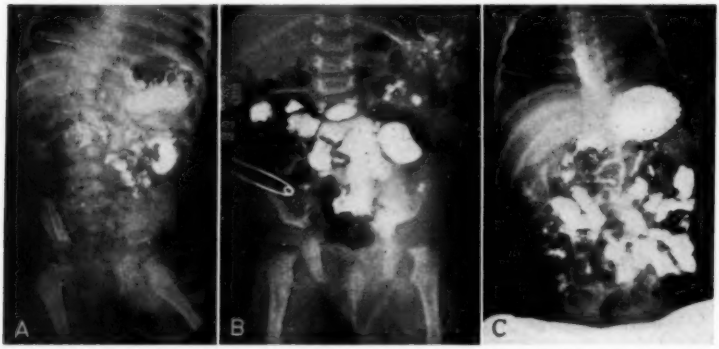

Fig. 35. Roentgenograms of the upper intestinal tract after a barium swallow in 3 different infants. A, Normal infant 6 months old. B, Three months old infant with allergic celiac syndrome. C, Four months old girl with allergic celiac syndrome.

Skin Tests. Only infrequently can one expect to find positive skin tests to the food which one feels certain clinically is responsible for these infants' diarrhea and other symptoms. One possible explanation[22] might be that local organ sensitivity might precede a generalized sensitivity when certain tissues of the body (e.g., the intestinal tract in this instance) may be sensitive, while other tissues (e.g., skin) are not sensitive. The presence or absence of positive skin reactions to the suspected offending food, however, may not have the importance many give to this finding. Lippard[13] showed that the presence of complement-fixing antibodies to a given food is not per se proof positive that a child is an atopic person. However, when present, P-K (passive transfer) antibodies are somewhat more suggestive of clinical sensitivity. Parke[21] in 1920 concluded essentially the same thing and stated that "evidence of its (allergy to a given food in question) existence, essentially equivalent to proof, may be furnished by *clinical data alone.*"

ADDITIONAL CLINICAL OBSERVATIONS

Most of the children with an allergic gastrointestinal affliction are remarkably well nourished and often have a good appetite. However,

some of the infants with the most severe acute gastroenteritis, particularly that due to cow's milk, may become severely emaciated and have a clinical picture strikingly similar to that in children with cystic fibrosis of the pancreas. Those described by Rubin[30] had a bloody diarrhea. Some infants have symptoms in the neonatal period or later in the first month of life. Others may have diarrhea in later months when wheat cereal or some vegetable is introduced into the diet. Rothman[27] points out that most of these children have a tendency to recover spontaneously from their gastrointestinal symptoms at two years of age.

DIFFERENTIAL DIAGNOSIS

The following diagnoses must be considered in any child with a chronic diarrhea:

Cystic Fibrosis of the Pancreas. These children may have steatorrhea in the first six months with or without the recurrent respiratory infections which subsequently lead to their death. Since it may appear to take a benign course for months or even years, this disease should be always kept in mind. It may be ruled in or out by one or all of the following measures: (1) an analysis of a fresh duodenal juice specimen for pancreatic enzymatic activity,[5] (2) an analysis of a fresh fecal specimen for trypsin activity,[8] and a study of vitamin A absorption.[17]

Idiopathic Infantile Steatorrhea. Many infants who are suspected of milk intolerance on an allergic basis appear to be greatly helped by a formula of skimmed milk. Although they have a definite steatorrhea, similar to that in infants with allergic celiac syndrome, cystic fibrosis of the pancreas and idiopathic celiac syndrome, they have no fecal eosinophilia and have a normal pancreatic trypsin and amylase concentration. Some of these children have minimal reduction in the lipase activity of their duodenal juice. They are helped by a low fat diet. This is probably one of the most common causes of chronic diarrhea in the first six months of age.

Idiopathic Celiac Disease. This syndrome usually begins in the second half of the first year of life. The vitamin A absorption curves resemble those of idiopathic infantile steatorrhea (see Fig. 34). Pancreatic enzyme concentrations are usually normal. These children will continue to have diarrhea for at least two years unless starch as well as fat is restricted from the diet.

Starch Intolerance. Children with a mild celiac syndrome due to starch intolerance have been described by Andersen.[2, 3] Though severe cases of idiopathic steatorrhea may show excess starch granules in the feces, the starch-laden stool of the patient with dietary starch intolerance has a normal fat content. The other characteristic features are a decreased amylase concentration in the fluid obtained by duodenal intubation and clinical improvement on a low starch diet.

Chronic Infectious Diarrhea. Although with our modern sanitary conditions typhoid and paratyphoid infections are rare in many cities, we have to think of the possibility of salmonellosis in small children with a chronic diarrhea. These children may have a steatorrhea or even a bloody diarrhea. Some of them become so emaciated from a concomitant salmonella sepsis that they have other severe metabolic and electrolyte disturbances seen in the most severe incidences of idiopathic celiac disease, cystic fibrosis of the pancreas or the bloody diarrheas of allergic origin. Careful bacteriologic study of the feces together with serum agglutinations usually makes the diagnosis definite.

Giardia Infestation. Children infested with the intestinal parasite, *Giardia intestinalis,* tend to have loose, excessive amounts of fat[31] in their feces. Katsampes and co-workers[11] demonstrated poor vitamin A ester absorption in these children. It has been suggested that this fecal steatorrhea results from the coating of the small intestine by these organisms, which are thought to act thus as a physical barrier to fat absorption. Treatment of the giardiasis with Atabrine has been noted[19] to be followed by a disappearance of the steatorrhea.

Other Less Common Causes of chronic diarrhea and steatorrhea may result from the following: infectious hepatitis, congenital obstruction of the pancreatic or bile ducts, excessive formation of insoluble soaps in the upper intestines, intestinal tuberculosis, malignant lymphoma, involvement of intestinal nodes, malrotation of the intestines, gastrocolic fistula, galactosemia and, rarely, adrenocortical insufficiency.

TREATMENT

Although one obviously should eliminate the offending food from the infant's diet as soon as one feels certain of the diagnosis, identification of exactly which food is responsible may not be so simple, even after it has been reasonably definitely established that the child's gastrointestinal symptoms are on an allergic basis. If the infant's diet consists of only a few foods, the history may suggest after which food introduction the symptoms began. If in doubt, a fairly safe procedure is to try an elimination diet free of wheat, milk, eggs and meats such as have been recommended by Rowe.[28] As in any elimination diet, one must not take away foods one at a time until the desired effect is achieved. Rather, one should start with the basic elimination diet. Although some students of this disease recommend starting with simply a low fat diet consisting chiefly of skimmed milk, rice and apple sauce on the theory that simple infantile steatorrhea is much more common than allergic celiac syndrome or other allergic diarrheas, the author is inclined to agree with Rowe[29] that the elimination diet is the procedure

of choice. Rowe feels that his elimination diets should be used not only as a therapeutic tool, but also as a *diagnostic* tool when one is in doubt as to which food is the offender or even if one is in doubt whether *any* food allergy exists. No matter which dietary approach is used, there should never be any excuse for failing to maintain adequate vitamins, protein and minerals in the diet to provide for adequate growth and development.

REFERENCES

1. Andersen, D. H.: Cystic Fibrosis of the Pancreas and Its Relation to Celiac Disease. Am. J. Dis. Child., 56:344, 1938.
2. Andersen, D. H.: Pancretic Enzymes in the Duodenal Juice in the Celiac Syndrome. Am. J. Dis. Child., 63:643, 1942.
3. Andersen, D. H.: Starch Intolerance, in Brennemann, J., ed.: Practice of Pediatrics. Hagerstown, Md., W. F. Prior Company, 1944, Vol. 1, Chap. 29.
4. Andersen, D. H.: Celiac Syndrome. VI. The Relationship of Celiac Disease, Starch Intolerance and Steatorrhea. J. Pediat., 30:564, 1947.
5. Andersen, D. H., and Early, M. V.: Method of Assaying Trypsin Suitable for Routine Use in Diagnosis of Congenital Pancreatic Deficiency. Am. J. Dis. Child., 63:891, 1942.
6. Fries, J. H., and Mogil, M.: Roentgen Observations on Children with Gastrointestinal Allergy to Foods. J. Allergy, 14:310, 1943.
7. Gibbs, G. E., Bostick, W. L., and Smith, P. M.: Incomplete Pancreatic Deficiency in Cystic Fibrosis. J. Pediat., 37:320, 1950.
8. Johnstone, D. E.: Studies on Cystic Fibrosis of the Pancreas; Role of Various Diluents and the Dilution Factor in the Interpretation of the X-ray Film Test for Fecal Trypsin. Am. J. Dis. Child., 84:191, 1952.
9. Johnstone, D. E.: Allergic Diarrheas and Their Relation to the Celiac Syndrome. Presented at the Pediatric Allergy Luncheon Roundtable, Tenth Annual Congress of the American College of Allergists, Miami Beach, April 9, 1954.
10. Johnstone, D. E., and McCoord, A. B.: Studies on the Absorption of Vitamin A in the Allergic Celiac Syndrome. Read by title at the meeting of the Society for Pediatric Research, Atlantic City, May 5, 1953.
11. Katsampes, C. P., McCoord, A. B., and Phillips, W. A.: Vitamin A Absorption Test in Cases of Giardiasis. Am. J. Dis. Child., 67:189, 1944.
12. Kunstadter, R. H.: Gastrointestinal Allergy and the Celiac Syndrome. J. Pediat., 21:193, 1942.
13. Lippard, V. W.: Immunologic Response to Ingestion of Foods by Normal and by Eczematous Infants. Am. J. Dis. Child., 57:524, 1939.
14. Lowe, C. U., and May, D. C.: Selective Pancreatic Deficiency. Am. J. Dis. Child., 82:450, 1951.
15. Lowe, C. U., May, C. D., Stauffer, H. M., and Neuhauser, E. B. D.: Fibrosis of the Pancreas, Enterogastrone and the "Duodenal Mechanism." Am. J. Dis. Child., 79:91, 1950.
16. McCoord, A. B.: Personal communication.
17. McCoord, A. B., and others: The Absorption of Oily and Aqueous Preparations of Ester and Alcohol Vitamin A by Normal Children and Children with Various Diseases. Pediatrics, 2:652, 1948.
18. McKhann, C. F., Spector, S., and Meserve, E. R.: Association of Gastrointestinal Allergy with Celiac Syndrome. J. Pediat., 22:362, 1943.
19. Maris, E. P., and Bushong, S.: The Diagnosis of *Giardia Intestinalis* Infestation by Means of Intestinal Intubation. The Treatment with Atabrine and Follow-up Studies of 68 Cases. Pennsylvania M. J., 45:724, 1942.
20. Nance, F. D.: Stool Eosinophilia in Gastrointestinal Allergy. J. Pediat., 33:313, 1948.

21. Parke, E. A.: A Case of Hypersensitiveness to Cow's Milk. Am. J. Dis. Child., *19*:43, 1920.
22. Ratner, B.: Abdominal Pain in Children Due to Allergy. J.A.M.A., *127*:696, 1945.
23. Ratner, B., and Silberman, D.: Allergy—Its Distribution and the Hereditary Concept. Ann. Allergy, *10*:1, 1952.
24. Ratner, B., Jackson, H., and Gruehl, H.: Transmission of Protein Hypersensitiveness from Mother to Offspring. V. Active Sensitization in Utero. J. Immunol., *14*:303, 1927.
25. Riley, I. D.: Metabolic Eczema in Idiopathic Steatorrhea. Lancet, *1*:262, 1939.
26. Rosenblum, A. H., and Rosenblum, P. P.: Gastrointestinal Allergy in Infancy. Pediatrics, *9*:311, 1952.
27. Rothman, P.: Diarrhea of Allergic Origin. Am. J. Dis. Child., *86*:201, 1953.
28. Rowe, A. H.: Elimination Diets and the Patients' Allergies. Philadelphia, Lea & Febiger, 1944, pp. 178–183.
29. Rowe, A. H.: Personal communication.
30. Rubin, M. I.: Allergic Intestinal Bleeding in the Newborn; Clinical Syndrome. Am. J. M. Sc., *200*:385, 1940.
31. Veghelyi, P.: Giardiasis in Children. Am. J. Dis. Child., *56*:1231, 1938.

220 Meigs Street
Rochester 7, N.Y.

NEUROLOGIC ALLERGY IN CHILDHOOD

SUSAN C. DEES, M.D.

As experience with allergic conditions increases, we recognize more frequently that allergic reactions may affect the nervous system. No part of the central nervous system is immune from such a response, given the proper situation and stimulus. These reactions occur in children as well as adults, although the majority of reported cases are those of adults. This is true, not because children have less vulnerable nervous systems than adults, but because children are less articulate in describing sensations and situations which vary from their usual state. Furthermore, neurologic examination is more difficult and more often cursory in children than in older people. The most comprehensive report on this subject is that of Davison,[10] who summarized his personal cases and reviewed the literature to 1952.

DIAGNOSIS

In allergy involving the nervous system, as with allergy elsewhere, the allergic reactions may require reinforcement by nonspecific factors to become manifest. These may be physical depletion, fatigue, chilling, infection, nonspecific irritants, hormonal changes, psychogenic stimuli and previous trauma. The nervous system has certain fixed reaction patterns to noxious substances, and the same central nervous system response may be elicited by different allergens and nonallergenic causes in the same person. For this reason it may at times be difficult to prove the allergic nature of symptoms and signs involving the central nervous system.

Convulsive disorders,[9, 27, 34, 41] headache,[8, 43] meningitis[36] and

From the Department of Pediatrics, Duke University Medical School, Durham, N.C.

cranial[16, 26, 31] and peripheral[47] nerve palsies are the clinical conditions most frequently seen and reported as being due to allergic reactions. The encephalitic[13, 19, 29] syndromes, certain degenerative conditions of the central nervous system,[18, 25] behavior disorders[11, 27] and cyclic vomiting at times may be unusual allergic reactions of the nervous system, but rarely is their allergic or other etiology fully and definitely established.

HEADACHE

Headaches which are allergic in origin are probably the commonest forms of allergy of the central nervous system. Stoesser[40] found forty-nine children with migraine among 750 children with headache (6.5 per cent), although their exact frequency is difficult to determine.[2, 17, 23, 42] Young children frequently complain of headache which is poorly localized and rarely hemicranial in distribution. Somnolence, preceded or followed by nausea and vomiting, is a common accompaniment of headache. Photophobia is present in some children.

If the child has an allergic rhinitis, it may be difficult to distinguish between headache caused by the acute change in pressure within the sinuses due to allergic edema, so-called vacuum headache,[35] and a headache intracranial in origin. "Vacuum" type of headache may be associated with tenderness on pressure over the sinuses. It is frequently and dramatically relieved by a potent antihistaminic, or vasoconstrictor locally applied. Such headaches often occur in the hay fever season.

If the headache is migraine-like, a pattern of recurrence is soon established, and as the child grows older, the prodromal symptoms characteristic of migraine become obvious. The child is apt to be irritable, hyperactive and unreasonable, or excessively subdued at the onset. Appetite may be perverted from normal; constipation may be present. Some children have been observed to gain weight rapidly just prior to the headache, and to lose it just as rapidly as the headache wanes. Diuresis or enuresis may be present at this time. In our experience the visual symptoms of scotomas, flashes of light, diplopia and hemianopsia are rarely noted in children under eight or nine years of age. This absence is probably due to the child's inability to describe these strange sensations and to our tendency to get the history from the parent, and not by directly questioning the child, rather than to the fact that they do not occur in children. If we listen to the child, he may tell us he sees "bees" or "flies" or lights, or indicate that he has diplopia, and these symptoms should alert us to the likelihood that he has migraine.

Physical examination usually is unrevealing except for the appearance of acute discomfort and unresponsiveness. The eyegrounds are normal; the neurologic examination is physiologic. Laboratory studies of blood

and urine contribute no abnormal characteristic findings. The electroencephalogram with spiky wave changes which have been observed in adults has not been reported in children, probably because records have not been obtained during or in the prodromata of a headache.

How, then, does one diagnose migraine in children? The diagnosis is often not made until the recurring pattern becomes crystallized and reminds the parents or physician of other persons, often relatives, who have migraine. During this period of observation one will have eliminated all the other logical causes of such headaches, particularly brain tumor, or other intracranial space-occupying lesions.

The drug therapy of migraine in children is similar to that of adults except for modification of dosage to suit the age and size of the patient. Aspirin may be effective with children, perhaps because it is sedative as well as analgesic. For many children Caffergone,[24] a combination of caffeine (100 mg.) and ergotamine tartrate (1 mg.), 1 tablet or rectal suppository at onset of headache, repeated in one hour if necessary, and in two to three hours for a total of four doses, gives prompt relief. At times ergotamine tartrate hypodermically or sedation with barbiturates may be needed to make the discomfort bearable. It is usually wise to restrict fluids for about six hours after the onset to minimize vomiting.

The allergic study of migraine usually involves skin testing to foods and, at times, other allergens, but is apt to give negative or equivocal reactions. Any clues obtained by this technique are worth investigating with elimination diets and food diary records. The latter are of greatest value even without preliminary testing. Parents are instructed to record everything the child has eaten for the two days preceding a headache. If such a record is kept and compared as headaches recur, it may be apparent that one or two foods constantly recur in the diet just prior to the headache. The role of these suspicious foods may then be more simply investigated by comparing symptoms during periods of controlled trial feeding, and avoidance. The precision with which one identifies a causative allergen in migraine is directly related to the persistence and skill of the doctor and parents as medical detectives. There are many persons with migraine or migraine-like headaches which are not allergic and for which no specific cause is ever found. In such children a family history of similar trouble is common, and emotional stress seems to be a common inciting factor.

CONVULSIVE DISORDERS

Convulsive disorders due to allergy have been observed in children as well as adults. This cause has been accepted reluctantly by some,[4] but an impressive number of well documented cases have been reported since those of Thompson,[41] Ward,[45] and Shannon,[34] so that by 1952

Davison[10] had collected 110 such patients with allergic epilepsy from the literature in addition to sixty-seven personal cases.

Allergy may be related to a convulsive disorder in two ways: (1) indirectly, as is any depleting, nonspecific physical abnormality, or (2) directly, by a specific allergen reacting in the central nervous system with or without simultaneous allergic reactions in other more common shock organs such as the skin or lungs. The first type is found most often, and in these patients the cause and control are apt to be difficult to effect, since the relationship is not always clear-cut. Children who have the second type of allergic convulsive disorder are rare and comprise a small percentage of the total with idiopathic epilepsy.

We have found a modification of Forman's[20] criteria for suspecting allergic epilepsy most helpful. They are as follows: (1) family or personal history of allergy, (2) eosinophilia preceding and during attacks, (3) positive skin tests, (4) absence of demonstrable organic brain disease, (5) characteristic electroencephalographic pattern of occipital dysrhythmia.

Our studies[14] of the electroencephalograms of allergic children have shown a high percentage of one type of abnormality, namely, occipital dysrhythmia, or irregularity, in children with allergy alone and with neither past history of nor present convulsions. This finding has been confirmed by others who have studied patients with atopic dermatitis[39] and with asthma.[6] We believe electroencephalographic abnormality is a frequent finding in allergic children and should be included in the criteria mentioned, as one more objective test for aiding in establishing a diagnosis of allergic epilepsy.

Dees and Lowenbach[13, 15] have reported two subsequent studies on children with epilepsy. In the first, a group of thirty-seven allergic children with convulsive disorders of grand or petit mal type showed occipital dysrhythmia as the predominant abnormality in seventy-three per cent of the records. In a control series of twenty-three nonallergic children with convulsions, only two, or less than 10 per cent, had occipital dysrhythmia.[13]

In the allergic group of thirty-seven, antiallergic measures were followed by such a good control of convulsions in twenty-four patients that withdrawal of sedatives was possible in twelve patients. These results are summarized in Table 33.

Case I. An illustrative case of specific sensitivity from this initial series of allergic children who has now been followed for 9 years is that of C.R., who is milk sensitive and has grand mal seizures.[15] Frequent petit mal episodes began just before he was 5 years old and lasted 1 year. "Colitis" and diarrhea developed during this period and were present until he was 6 years old. From 6 to 7 years of age he was on a completely milk-free diet and was perfectly well. At 7 years he resumed a full diet, and almost at once diarrhea and grand mal developed. A milk-free diet for nearly 2 asymptomatic years was followed again by grand mal when milk was again tried in 1945 at

age 9½ years. The electroencephalogram at this time showed occipital dysrhythmia. A second electroencephalogram in 1946, nearly a year after milk had again been discontinued, showed definite improvement with a record within normal limits. The night before this electroencephalogram was made, for the first time in a year he had broken his diet by eating ice cream and had had, during sleep, a mild generalized con-

TABLE 33. *Results of Antiallergic Treatment in 37 Children with Convulsive Disorders*

	PATIENTS WITH CONVULSIONS		NUMBER OF PATIENTS IMPROVED	PATIENTS REQUIRING SEDATION	
	Before Allergy Treatment	After Allergy Treatment		Before Allergy Treatment	After Allergy Treatment
Patients with clinical allergy	22	4	18	20	9
Patients with no clinical allergy	15	9	6	15	14
Total	37	13	24	35	23

From S. C. Dees and H. Lowenbach: Allergic Epilepsy. Ann. Allergy, Vol. 9.

vulsion. Because of this dietary lapse and the convulsion, the consulting neurologist prescribed Mebarol and Dilantin. These anticonvulsants and a less restricted diet were used for one year, during which the child was clinically well. Sedation was discontinued when the patient was 11½ years old. Within a few weeks on a general diet the child became irritable and inattentive with recurrent petit mal. Milk again was discontinued completely for 4 asymptomatic years.

At the age of 15 years he had a herniorrhaphy. During his hospital convalescence his parents reported to us that he had several mild generalized convulsions for a period of 3 days while on a surgical soft diet containing milk. These promptly stopped, without recourse to sedation, when milk was discontinued. He was last examined by us just before he was 17 years of age, at which time he still was avoiding milk. He had no abnormal physical findings except acne and no complaints. Because he felt so well and was convinced that he is milk-sensitive, he refused to permit an electroencephalogram at this visit. A portion of this patient's record is summarized in Figure 36.

CASE II. A child who illustrates less specific sensitivity is J.S., who had improvement of petit mal when an accompanying allergic rhinitis was controlled. He was 7 years old when first seen, having had innumerable petit mal seizures daily for the past 3 years, which were not decreased while on Tridione. In addition he had perennial allergic rhinitis, with skin sensitivity to pollens and animal danders. During 3 years of desensitization to pollen, and no close animal contact, he had almost no nasal symptoms. During his first year the dosage of Tridione which had previously not controlled symptoms was continued, and he had *no* petit mal. The drug was then discontinued, and on the allergy regimen only he remained free of petit mal. He then became tired of desensitization and insisted on acquiring a dog. Both allergic rhinitis and petit mal recurred. His initial electroencephalogram showed occipital dysrhythmia which improved during his symptom-free period and while off Tridione, and which recurred with his clinical relapse.

From these reported studies and from our additional unpublished observations we believe that a significant number of allergic children

have electroencephalographic patterns which deviate from the normal records seen in nonallergic children of comparable age. In addition, there is a striking preponderance of dysrhythmia localized in the occipital areas. This finding is not specific for allergy, since it occurs in a variety of other conditions, as well as in some apparently normal children. Nor is it necessarily an indication of a convulsive tendency, since it is present in children who have never had convulsions. The importance of this association of occipital dysrhythmia with allergy is to

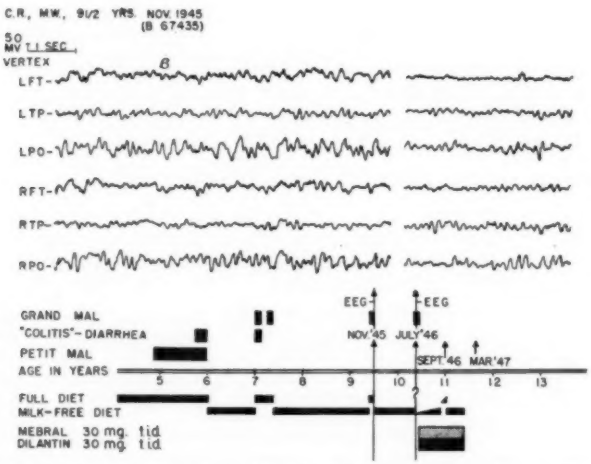

Fig. 36. Clinical course of a milk-sensitive child with grand mal seizures. (From S. C. Dees and H. Lowenbach: Allergic Epilepsy. Ann. Allergy, Vol. 9.)

serve as a reminder to study allergic symptoms, which may be secondary complaints and would otherwise be neglected in the attention focused on the primary convulsive problem.

The investigation of a child with epilepsy who has frank or suggestive allergy is carried out exactly as one would study any allergic problem. The treatment should be planned as indicated by the probable allergies unearthed. Suspected foods should be avoided, and inhalant and pollen sensitivities should be controlled by avoidance and desensitization. Parents should be instructed to keep complete records of the child's exposure and diet at times when symptoms occur in order to discover additional allergens.

Our studies have not incriminated any one type of allergen in a majority of cases. Davison[10] analyzed causative agents in the patients reported in the literature as having proved allergic epilepsy, and found that foods were the commonest causes, milk, eggs, wheat and chocolate

accounting for most of the reactions. Inhalants and pollen were infrequent offenders in these patients.

We have not found antihistaminics effective in controlling seizures in these allergic children, even though they may completely relieve other allergic symptoms. A few children have had a decrease in electroencephalographic irregularities while taking antihistaminics.[7, 14]

MENINGEAL AND NEURITIC ALLERGY

The third general type of allergic reaction in the nervous system involves the meninges and the cranial and peripheral nerves. These are uncommon reactions usually due to sensitivity to serums,[21, 36, 44, 46] vaccine,[22] drugs[28] and infections.[19] A few instances of sensitivity to food,[38] physical agents[30] and inhalants[25] have been reported.

Ratner[32] reviewed such meningitic reactions and described three types of meningitis due to serum injection: (1) serum sickness meningitis, (2) aseptic or serum meningitis, and (3) allergic meningitis. The first type occurs during serum sickness and follows extrathecal injections of serum. Cerebrospinal fluid pressure, protein and lymphocytes are abnormally high. Symptoms are consistent with increased intracranial pressure and include headache, nausea, vomiting, coma and convulsions. Paralysis of the brachial plexus is common: neuritis or neuralgia involving other peripheral nerves occurs. Optic neuritis as the only finding or in conjunction with the other neurologic abnormality has been observed in this type.[31]

Aseptic or serum meningitis may immediately follow direct intrathecal injections of serum. Severe symptoms of central nervous system irritation rapidly develop, and the cerebrospinal fluid contains increased polymorphonuclear cells, although it is bacteriologically sterile.

Allergic meningitis develops after a latent period after intrathecal serum in a person previously sensitized to serum. Meningeal symptoms are fulminating and may be fatal if serum is not discontinued at once. Epinephrine, antihistaminics and fluids must be administered promptly.

Antibiotics have so largely supplanted serums in treating infections that these meningeal syndromes due to serums are decreasing. We have observed several patients in whom a similar allergic reaction occurred during combined intrathecal and intramuscular streptomycin treatment of tuberculous meningitis.

CASE III. One such previously reported patient,[12] a 4 year old boy, had received both intrathecal and intramuscular streptomycin for tuberculous meningitis. While still on intramuscular streptomycin, but several days after intrathecal treatment had been discontinued, he had an abrupt recurrence of meningeal symptoms. His cerebrospinal fluid just prior to this episode had been almost free of white blood cells and was sterile. With the recurrence of symptoms he had both blood and cerebrospinal fluid eosinophilia, with a rise in spinal fluid white blood cells, and negative cerebro-

spinal fluid culture. Streptomycin was temporarily discontinued and antihistaminics given, after which symptoms promptly subsided. It was then possible to reinstitute streptomycin therapy combined with antihistaminics without further symptoms.

CASE IV. A second patient had a sudden increase in total cerebrospinal fluid white blood cells, on the tenth day of combined intrathecal and intramuscular streptomycin therapy for tuberculous meningitis. Her meningeal symptoms were so severe from the onset that there was no apparent change in her clinical condition at this time. However, a differential stain of the cerebrospinal fluid sediment showed that practically all the white blood cells were eosinophils. Intrathecal streptomycin was decreased, and the cell count and eosinophilia decreased, although the drug was not discontinued entirely.

Similar eosinophilia on the seventh to tenth day of streptomycin therapy was noted in one other patient, an infant who expired shortly thereafter of tuberculous meningitis.

The usual technique for counting white blood cells in cerebrospinal fluid will not stain eosinophils, and it is only in unusual circumstances that a search is made for their presence, which may account for overlooking an allergic meningeal reaction.

Peripheral neuritis, chiefly of the brachial plexus, has occurred frequently after serum, particularly antitetanus serum. This usually follows serum sickness with urticaria; however, cases have occurred in which the neuritis was the only reaction. Typhoid vaccine and intramuscular penicillin have produced similar reactions, and many other vaccines and drugs have also been reported to be responsible.[28] The symptoms begin several days to two to three weeks after serum injections, often with paralysis; there may be associated paresthesias and pain. Neuritis lasts variable periods, often several months; if it is associated with muscle atrophy, the disability may be permanent. To our knowledge, the effectiveness of antihistaminics and ACTH or cortisone has been reported only sporadically in this connection, but it would seem reasonable to treat such neuritis in the early stages as one does other allergic disorders. Though the neurologic reactions due to rabies vaccine are not strictly comparable to those from these other agents, corticotropin therapy for rabies vaccine reactions has been reported to be effective in a few cases.[3] The remote possibility of neuritis, even in allergic children, is not a contraindication to the routine use of prophylactic immunizations.

The encephalitic syndromes have been reported to follow administration of drugs such as arsenic, sulfonamides, penicillin, streptomycin and other antibiotics;[28] vaccines too, particularly pertussis[5] and typhoid vaccine,[22] have been followed by encephalitis thought to be allergic. The postinfectious encephalitides frequently seen after measles, for example, may be in part an allergic reaction.[19] The effectiveness of ACTH in its treatment is by no means proof of an allergic factor, but is suggestive that further investigation of an allergic etiology should be carried out. Ferraro[18] studied two cases of postscarlatinal encephalitis, in which the

vascular reactions suggested allergic reactions in the brain. The encephalitis following injections of brain tissue which is produced experimentally has no exact counterpart in pediatric practice except in the reactions due to antirabies vaccine made from rabbit brain. This is an infrequent but dreaded sequel to rabies prophylaxis. Blatt and Lepper[3] found eight nervous system reactions among sixteen persons who had reactions to rabies vaccine in a series of 2193 treated patients. Three patients were treated with corticotropin, and in two recovery was rapid.

SUMMARY

To summarize the various aspects of neurologic allergy, one finds that migraine, selected cases of epilepsy, allergic meningeal reactions, cranial and peripheral neuritis are the most commonly reported conditions in children as well as adults. These varied reactions are due to an equally varied group of allergens, including drugs, serums, vaccines, foods, infections, physical agents and airborne allergens. Most of these neurologic disorders tend to occur in allergic persons, are less consistent in their anatomic distribution than are organic diseases, are of short duration, and are reversible. They frequently respond to the same type of treatment as does allergy elsewhere in the body. To be accepted incontrovertibly as allergic, one must have not only excluded all likely organic etiology, but also have established the allergic character of the process by fulfilling the usual criteria for allergic diseases. This includes, in most instances, identifying the allergen and reproducing symptoms on exposure and relieving them on withdrawal on several controlled occasions. This aspect of allergy is most rewarding from the diagnostic and therapeutic standpoints and warrants giving neurologic allergy more serious and widespread attention than it often receives.

REFERENCES

1. Baker, A. B., and Noran, H. H.: Changes in the Central Nervous System Associated with Encephalitis Complicating Pneumonia. Arch. Int. Med., *76*:146, 1945.
2. Balyeat, R. M., and Rinkel, H. J.: Allergic Migraine in Children. Am. J. Dis. Child., *42*:1126, 1931.
3. Blatt, N. H., and Lepper, M. H.: Reactions Following Antirabies Prophylaxis. Am. J. Dis. Child., *86*:395, 1953.
4. Bridge, E. M.: Epilepsy and Convulsive Disorders in Children. New York, McGraw-Hill Book Co., Inc., 1949.
5. Byers, R. K., and Mall, F. C.: Encephalopathies Following Prophylactic Pertussis Vaccine. Pediatrics, *1*:437, 1948.
6. Chobot, R., Dundy, H. D., and Pacella, B. L.: The Incidence of Abnormal Electroencephalographic Patterns in Allergic Children. J. Allergy, *21*:334, 1950.
7. Churchill, J. A., and Gammon, G. D.: The Effect of Antihistaminic Drugs in Convulsive Seizures. J.A.M.A., *141*:18, 1949.

8. Clarke, T. W.: Neuro-allergy in Childhood. New York State J. Med., 48:393, 1948.
9. Clein, N. W.: Epilepsy of Allergic Origin. Northwest Med., 36:378, 1937.
10. Davison, H. M.: Allergy of the Nervous System. Quart. Rev. Allergy, 6:157, 1952.
11. Dees, S. C.: Inter-relationships of Allergic and Psychosomatic Factors in Allergic Children. Woods School Bull. No. 12: 59, 1945.
12. Dees, S. C.: Neurological Allergy, in Ratner, B.: Allergy in Relation to Pediatrics. St. Paul, Bruce Publishing Co., 1951, Chap. 9.
13. Dees, S. C.: Electroencephalography in Allergic Epilepsy. South. M. J., 46:618, 1953.
14. Dees, S. C., and Lowenbach, H.: The Electroencephalograms of Allergic Children. Ann. Allergy, 6:99, 1948.
15. Dees, S. C., and Lowenbach, H.: Allergic Epilepsy. Ann. Allergy, 9:446, 1951.
16. Duke, W. W.: Ueber Meningitis Serosa. Samml. klin. Vortrage innere Medicin, 5:655, 1893.
17. Eyerman, C. H.: Allergic Headache. J. Allergy, 2:106, 1931.
18. Ferraro, A.: Pathology of Demyelinating Diseases as an Allergic Reaction of the Brain. Arch. Neurol. & Psychiat., 52:443, 1944.
19. Finley, K. H.: Pathogenesis of Encephalitis Occurring with Vaccination, Variola, and Measles. Arch. Neurol. & Psychiat., 39:1047, 1938.
20. Forman, J.: Atopy as a Cause of Epilepsy. Arch. Neurol. & Psychiat., 32:517, 1934.
21. Gardere, M., and Gaugolphe, M.: Nervite au cours d'un cas de tetanos traité par la serum thérapie. Lyon Méd., 110:497, 1908.
22. Gayle, R. F., Jr., and Bowen, R. L.: Acute Ascending Myelitis Following the Administration of Typhoid Vaccine: Report of a Case with Necropsy Findings. J. Nerv. & Ment. Dis., 78:221, 1933.
23. Goltman, A. M.: Mechanism of Migraine. J. Allergy, 7:351, 1936.
24. Hansel, F. K.: The Treatment of Headache. Ann. Allergy, 7:155, 1949.
25. Hurst, E. W.: Experimental Demyelination of the Central Nervous System. III. Poisoning with Potassium Cyanide, Sodium Azide, Hydroxylamine, Narcotics, Carbon Monoxide, etc., with Some Consideration of Bilateral Necrosis Occurring in the Basal Nuclei. Australian J. Exper. Biol. & M. Sc., 20:297, 1942.
26. Jenkins, C. M.: Cerebral Oedema Due to Phenobarbital Sensitivity. Ann. Allergy, 7:346, 1949.
27. Kennedy, F.: Cerebral Symptoms Produced by Angioneurotic Oedema. Arch. Neurol. & Psychiat., 15:28, 1926.
28. Lane, S. L., Kutscher, A. H., and Segall, R.: Unusual Toxic Reactions to Sulfonamides and Antibiotic Therapy. A Review of the Literature from 1936–1953. Ann. Allergy, 11:615, 1953.
29. Lapin, J. H., and Mond, I.: Serum Sickness-Like Syndrome from Penicillin. Am. J. Dis. Child., 82:335, 1951.
30. McGovern, J. P.: An Unusual Case of Hypersensitivity to Cold Complicated by Paroxysmal Diarrhea. J. Allergy, 19:408, 1948.
31. Mason, V. R.: Optic Neuritis in Serum Sickness. J.A.M.A., 78:88, 1922.
32. Ratner, B.: Allergic Manifestations in the Central Nervous System. Am. J. Dis. Child., 75:747, 1948.
33. Scott, T. F. McN., Coriell, L., Blank, H., and Burgoon, C. F.: Some Comments on Herpetic Infection in Children with Special Emphasis on Unusual Clinical Manifestations. J. Pediat., 41:835, 1952.
34. Shannon, W. R.: Neuropathic Manifestations in Infants and Children as a Result of Anaphylactic Reactions to Foods Contained in the Dietary. Am. J. Dis. Child., 24:89, 1922.
35. Sheldon, J. M., Lovell, R. G., and Matthews, K. P.: A Manual of Clinical Allergy. Philadelphia, W. B. Saunders Company, 1953, p. 233.
36. Sheppe, W. M.: Reaction of the Meninges to Therapeutic Serum. Am. J. Clin. Path., 1:77, 1931.

37. Spangler, R. H.: Some Allergic Factors in Essential Epilepsy. J. Allergy, *1*:39, 1931.
38. Staffieri, D., Bentolila, L., and Levit, L.: Hemiplegia and Allergic Symptoms Following Ingestion of Certain Foods: A Case Report. Ann. Allergy, *10*:38, 1952.
39. Sternberg, T. H., and Baldridge, G. D.: Electroencephalographic Abnormalities in Patients with Generalized Neurodermatitis. J. Invest. Dermat., *11*:401, 1948.
40. Stoesser, A. V., and Nelson, L. S.: Incidence and Treatment of Headaches Due to Allergy in Children. Presented before the American College of Allergists Meeting, Miami, April 9, 1954.
41. Thompson, J.: Clinical Types of Convulsive Seizures in Very Young Babies. Brit. M. J., 2:679, 1921.
42. Valquist, B., and Hackzell, G.: Migraine of Early Onset. Acta pædiat., *38*:622, 1948.
43. Vaughan, W. T.: Allergic Migraine. J.A.M.A., *88*:1383, 1927.
44. Walker, D. C.: Serum Neuritis Secondary to Tetanus Antitoxin. Bull. Springer Clin., Tulsa, Okla., 3:3, 1952.
45. Ward, J. F.: Protein Sensitization as a Possible Cause for Epilepsy and Cancer. New York Med. J. Rec., *115*:592, 1922.
46. Winkleman, N. W., and Gotten, N.: Encephalomyelitis Following the Use of Serum and Vaccine. Report of Two Cases, One with Autopsy. Am. J. Syph. & Neurol., *19*:414, 1935.
47. Young, F.: Peripheral Nerve Paralysis Following the Use of Various Serums. J.A.M.A., *98*:1139, 1932.

Duke University Hospital
Durham, North Carolina

THE ALLERGIC TENSION-FATIGUE SYNDROME

FREDERIC SPEER, M.D.

One of the most significant developments in contemporary medicine has been the increasing recognition that the soma and the psyche are not distinct and unrelated, but are so closely bound together as to make proper investigation of both a necessary part of the management of disease. As a result, the psychosomatic approach is now used in a wide field of medicine, with so much enthusiasm, in fact, that it is often forgotten that this relationship may operate in the opposite direction, and that somatic disease may often be the cause of disorders of feeling and behavior rather than the effect. This especially applies in pediatric practice, in which the patient's ability to express his complaints is limited and an organic basis for nervous manifestations may easily be overlooked. Among the many somatic factors which may be manifested in behavior disturbances is allergy, and it is the purpose of this paper to discuss the behavior pattern characteristic of certain allergic children.

HISTORICAL DEVELOPMENT

That allergy may be responsible for vagaries of behavior was noted in the early days of allergy. In 1916 Hoobler[7] described a group of allergic children as "restless, fretful, and sleepless." He recognized the clinical importance of these manifestations, commenting, "Among several of my cases this was the outstanding characteristic and was the condition for the alleviation of which I was consulted." In 1922 Shannon[22] published the first report which recognized that nervous system disturbances could at times constitute a primary allergic syndrome. He implicated certain foods as etiologic agents in irritability, insomnia and general "nervousness." That he did not consider such findings merely secondary to other allergic disturbances is revealed in this strongly worded observa-

tion: "The symptoms were those of the neuropathic diathesis without a history of frank exudative phenomena preceding!" The following year May[12] described unnatural somnolence as an allergic phenomenon, and in 1925 Piness[13] found the allergic child "vaguely nervous, irritable, and difficult to control."

An important contribution was made by Kahn[9] in 1927. He recognized that many children with pollinosis suffered from a constitutional state independent of hay fever or asthma. His description is vivid and timely: "Languidness and restlessness are the rule, alternating with spells of intense temper and fury. These children are almost invariably extremely cross and irritable, resisting all handling, and crying on the slightest provocation." In 1930 Rowe[19] reported at length on nervous manifestations and toxemia in allergic adults as well as children. His findings have been confirmed and expanded by Davison,[5] Kaufman[10] and Randolph.[15] Excellent descriptions of the manifestations peculiar to children have been contributed by Randolph[16] and Clarke,[2, 3] and much of the credit for a revival of interest in the effect of allergy on the behavior of children is due to their work.

CLINICAL PICTURE

The workers in this field have used a variety of descriptive terms. Shannon described "neuropathic manifestations," and Kahn reported "pollen toxemia." Clarke speaks of "character problems due to allergy." Rowe and Randolph of "the allergic fatigue syndrome" or "allergic toxemia," Davison of "cerebral allergy," and Kaufman of "the allergic mental syndrome." This multiplicity of terms may give the first impression that the behavior pattern of allergic children is diffuse and vague, but closer study will reveal that the symptoms fall into two distinct categories. The first represents evidences of irritability and hyperkinesis and is termed *tension*. The second category includes sluggishness, torpor and other manifestations of lessened activity and is called *fatigue*. Tension and fatigue occur in varying degrees in different patients, but both are present in virtually all cases.

Tension

According to Pounders,[14] "the nature of the allergic child's trouble seems to make him restless, overactive, apprehensive, and antisocial at times." Parents usually describe such children as nervous, jittery or high-strung. Considerable confusion in terms may be avoided if it is recognized that tension consists in a blend of hyperkinesis and hyperirritability. Hyperkinesis is often noted early in life, the mother remarking that the child was always restless and inclined to "fight sleep." Through-

out the first three or four years of life this intense restlessness remains the outstanding characteristic, and, as would be expected, insomnia is a frequent problem.

As the child grows older, hyperirritability becomes increasingly manifest. The emotional balance is precarious, and the child is easily upset, characteristically crying readily and for long periods. These youngsters are almost universally regarded as "spoiled," even by their parents, who wonder where their methods of child care have been faulty. In some cases the patient is *aggressively* irritable and is described as ill-natured, resentful, domineering, and slow to forgive. Clarke[2] has pointed out that this behavior may border on the psychotic. In other cases the patient is described as timid and sensitive, and his parents will find that any correction must be mild lest he be thrown into a state of the greatest agitation. Mothers of these tense children seem to sense that the problem is one of mood and that the child is not delinquent, saying, "He isn't exactly naughty, just nervous!"

Fatigue

Since allergic tension may appear to represent little more than an exaggeration of the natural exuberance of childhood, it is likely to cause more exasperation than alarm. However, a persistent state of listlessness and fatigue is quite another matter, and when children behave in this way, parents soon seek medical help. Fatigue of allergic origin is not radically different from the malaise or vague indisposition common to many other conditions, but it has certain peculiarities that make a description useful. It is inclined to take one of two forms, and these will be discussed separately.

In the first type the patient suffers from a certain lethargy or sluggishness. There is commonly great difficulty waking from sleep, and for some time afterward the child is especially torpid. Occasionally the degree of apathy interferes with the child's progress in learning, but more commonly he manages to compensate quite well. When this peculiar listlessness is combined with such manifestations of tension as ill temper or oversensitiveness, the child is miserable indeed.

In the second type of allergic fatigue the child appears tired rather than sluggish. Even young children will follow their mothers about, complaining of being tired, and may come in from play to lie down. Randolph[15] pointed out that, unlike physiologic fatigue, this symptom is characteristically made worse by rest.

Achiness

Vague, widespread aching apparently represents fatigue in a more severe form. Leg ache is the most common complaint, but older chil-

dren complain at times of aching of the back, arms and neck. Leg ache is inclined to appear after the child has gone to bed and may be severe. At times there is aching about the knee, and there is natural concern in the parents' minds about the possibility of rheumatic fever.

PHYSICAL FINDINGS

Many of these children will not exhibit such frank evidence of allergic sensitization as eczema, asthma or hay fever, and physical findings may be meager. There are, however, a number of signs suggestive of a constitutional allergic state that are worthy of consideration. None is pathognomonic of allergy, but when they fit the total picture, especially if all are present, they are of diagnostic utility.

Hyperhidrosis

Bowen[1] describes certain asthmatic children as "wet sleepers." The excessive perspiration seen in some allergic children is severe. In infants it is especially marked about the head, while in older children the chest may be the prominent site. Mothers report that it is most noticeable shortly after the child has gone to bed.

Pallor

Anemic or not, allergic children are often pale. This fact was stressed by Kahn, who said, "The complexion is sallow or of a saffron tinge." A common by-product is "dark circles" of bluish or deep red discoloration under the eyes. It is probable that this phenomenon depends on the skin pigment and deep veins being thrown into relief by the blanching of surface vessels.

nfraorbital Edema

In a pioneer paper on pediatric allergy Schorer[21] described "puffiness under the eyes" in an allergic child. This is described by Randolph[16] as "an edematous, discolored appearance of the infraorbital areas." When combined with pallor and "dark circles," a typical facies is presented (Fig. 37). The edema is largely confined to the area of the malar prominences, while edema of the lids is minimal if present at all.

DIFFERENTIAL DIAGNOSIS

The etiologic possibilities that must be considered in the case of the child who is restless and listless are almost without limit.[20] An attempt will be made to outline some of the more common ones.

Disorders of the Nervous System. The importance of psychic factors in the production of behavior problems is a major study in itself, and no effort to enlarge on this subject will be made in this discussion. Perhaps less likely to be appreciated is the importance of organic factors in the nervous system. The postencephalitic state[6] is one example, and cerebral palsy and psychomotor epilepsy are others. The early findings in intracranial tumor may be obscure, and mild degrees of mental retardation are capable of producing a puzzling behavior pattern.

Malnutrition. Florid malnutrition is not a frequent problem where food is abundant, but borderline deficiencies are not infrequent and may be associated with vague symptoms. Lynch and Snively[11] have reported irritability, listlessness and pallor from a persistently low protein intake. A similar picture is seen in iron deficiency anemia, a common condition of young children which is easily overlooked.

Endocrine Dysfunction. As in the field of nutrition, borderline states of endocrine deficiency may be more important than has been generally appreciated. Mild degrees of hypothyroidism are well known to internists and obstetricians, but have been largely ignored in pediatrics. Recently Ratner[17] has reported "fatigue, poor scholarship, irritability, poor nutrition and susceptibility to colds" in cases of mild hypothyroidism. Diabetes is worthy of mention, but, because of the stormy course characteristic of the untreated disease in children, it is not easily overlooked.

Infection. Subacute and chronic infections are a constant possibility in the differential diagnosis of children with obscure complaints. Among the most important is urinary infection, especially in young girls. Infection in the paranasal sinuses and lymphoid tissue, although less common in the antibiotic era, is still important. There is a strong tendency away from tonsil removal, but Clein[4] reminds us that tonsillectomy often relieves "the dull feeling, fatigue, and general irritability common in children with hypertrophic infected tonsils." Other infectious diseases to be considered are infectious mononucleosis, malaria, tuberculosis and undulant fever.

Several other diseases belong in a discussion of the differential diagnosis of children with indefinite symptoms. None are more capable of presenting an obscure picture than rheumatic fever and chorea, but fortunately their prevalence and importance are well known. Consideration should be given to hidden handicaps such as visual or hearing loss. Early leukemia is another possibility. An unrecognized case of lymphatic leukemia in the writer's experience was referred to psychiatry as a behavior problem of psychic origin. A more pointed reminder of the necessity of *first* considering somatic influences in disturbed children cannot easily be imagined.

CASE HISTORIES

Case I. A. S., a 3 year old boy, was first seen in September, 1950, because of asthma. His parents were from Minnesota and were touring the country in a trailer, hoping to find a climate that would agree with him. He had a history of eczema, beginning at 3 months, which was thought to be due to egg. At 6 months a diagnosis of asthma was made, and attacks of great severity had occurred every 4 or 5 weeks since. His mother noticed that asthma tended to come on when he played with a cat or when he was around farm buildings. He had always been inclined to perspire excessively and often had a heat rash. His mother felt that he was never really well, but was inclined to fatigue, restlessness and tantrums. Although his attacks of ashma were severe, his parents were nearly as concerned about his high temper and lethargy.

In a clinic of dozens of children the patient stood out as remarkably wild and uncontrollable, and he was examined with the greatest difficulty. There was marked pallor and infraorbital edema. The nasal mucosa was swollen, pale and crusty, and the chest was hyperresonant with general expiratory wheezing. Scratch tests were positive as follows: mixed feathers, 3 plus; cat hair, 3 plus; wheat, 2 plus; Alternaria, 2 plus; and Hormodendrum, 2 plus.

Inhalent avoidance was instituted and mold hyposensitization was begun. Because egg had long been suspected, it was given a trial elimination of 4 days. When it was returned on the fifth day, a severe attack of asthma occurred. This test was repeated 10 days later with the same result. Egg has been avoided since, but accidental feedings have precipitated attacks on 2 occasions. When the asthma was well controlled, the mother remarked that there was little improvement in his disturbed behavior. Because of the positive reaction to wheat, this food was removed from his diet. Within 2 days there was almost complete relief of his customary tension and fatigue. He was contented and relaxed for the first time in months. With return of wheat on the fifth day there was complete relapse. In the intervening 3 years, attempts to return to wheat have been followed by the old torpor and restlessness. Difficult as it is to keep this highly allergic child on a diet which contains no wheat and egg, his parents have been more than glad to do so.

Comment. The clear separation of asthma and tension-fatigue is the remarkable feature of this case. Only with an intelligent and cooperative family can such a case be worked out. Also of interest is the fact that scratch tests were efficient in identifying wheat as a factor in nervous symptoms, while egg was identified by history and an individual food test.[18]

Case II. R. C., a boy, was first seen November 20, 1946, at the age of 5 days, because of violent colic. This was controlled slowly by milk modification. During his first year or so he was restless and sleepless, but was otherwise well until April, 1950, when he was brought in because he had become irritable, combative and difficult to manage. It was felt that his behavior disorder was of psychic origin, and the recent arrival of a baby sister was thought a probable factor. However, attention to his needs for affection and understanding was of no benefit, and by June he had become almost uncontrollable. About the same time he had a blocked nose, and allergy was then considered a possible cause of his complaints. In view of his early colic, an attempt to relieve him by milk abstinence was tried, but with no success. Skin tests were then done, and Alternaria was found to react 2 plus to a scratch test. Except for the typical allergic nasal mucosa, physical findings were negative.

Within 3 weeks of the time Alternaria hyposensitization was begun, this child was almost entirely relieved of his excessive irritability and incorrigibility. Somewhat more gradually his nasal symptoms subsided. His mother felt that she could about tell when hyposensitization injections were due by his increasing restlessness. At the end of the mold season in December his parents discontinued treatment, and he re-

mained well during the winter. The following April he presented himself for hyposensitization because of relapse in both nasal and behavior manifestations. He was successfully treated during this second season. During the season of 1953 the child did well, partly, it would seem, because of increasing immunity and partly because of the relatively low Alternaria counts during this drought year.

Comment. Most of what has been written about allergy as a cause of nervous disorders deals with food allergy, but in the writer's experience molds are of no little importance. Horesh[8] has reported on pollens as a cause of "fatigue, restlessness, loss of ambition, and dullness," and has found that many of these children later have hay fever.

CASE III. M. B., a boy, was first seen January 17, 1952, because of asthma. The diagnosis had been made 2 years previously by the family doctor, and the child was sent to Arizona. He was not relieved by this move, and he returned in November, 1951. Attacks occurred every 4 or 5 weeks and were severe and difficult to relieve. His nose was constantly blocked, and there was a persistent cough. Between attacks he was not well. He was persistently sluggish and tired, and if not aroused would sleep until noon. He was given to outbursts of temper and crying, and he complained of feeling "shaky all over." He often complained of aching of the arms and legs, especially the latter. There was a history of infant feeding troubles. He had been colicky on the breast, and when weaned at 6 months had difficulty retaining cow's milk.

When first examined, the child was not in an attack of asthma, but sibilant rales were heard on forced expiration. The nasal membranes were red and crusty, and there was considerable mucopurulent discharge. The skin was cold and clammy. The

Fig. 37. Allergic facies. A common manifestation of constitutional allergy which is seen in children with allergic tension-fatigue is infraorbital edema. Note that the swelling is most evident over the malar prominences. The facial pallor and "dark circles" frequently seen in allergic children are poorly shown in the photographs.

child was pale, and there was prominent infraorbital edema (Fig. 37, *a*). Scratch test reactions were as follows: Alternaria, 3 plus; house dust, 2 plus; and Hormodendrum, 2 plus.

Dust and mold avoidance was ordered, and house dust, Alternaria and Hormodendrum hyposensitization was begun. In view of his early colic and vomiting, milk was removed from his diet for 4 days. By the second or third day his state of tension and fatigue was almost totally relieved; when milk was returned the fifth day, he relapsed completely. This test has been repeated twice with the same result. Recovery from asthma has been uneventful, and as long as milk is avoided, the child is happy, alert and contented.

Comment. This case represents a type of tension-fatigue which is quite disabling. This youngster was practically an invalid, not merely

because of asthma, but because he was persistently tired, disagreeable and listless.

CASE IV. W.K., a boy, born December 11, 1947, has been under the writer's care since he was adopted at the age of one week. His infancy was uneventful. At the age of 12 months he began to be restless and seemed unable to relax enough to take naps. About the same time his stools began to be hard, and he was "gassy." He was no longer happy, but had become whiny and cross. His mother had noted a gradual increase in milk intake and a corresponding drop in appetite for solids. He had always tended to perspire easily, and in recent months this had become much more severe. At this time physical examination was negative. The combination of tension, insomnia and constipation with increased milk intake threw suspicion on that food. The child was put on soy milk (Mullsoy), and milk products were removed from the diet. This maneuver was followed by prompt improvement in the child's behavior. He was sleeping all night by the third night and was again happy and calm. His appetite improved greatly, and his stools became normal. A return to milk one week later slowly brought about a return of nervous and gastrointestinal difficulties. Several attempts to go back to milk have produced the same result.

The child remained well until the age of 3 years. About this time his disposition underwent a gradual change. His usually sunny disposition disappeared, and he became increasingly hard to manage. Investigation of his environment failed to show faults in parent-child relations. Physical findings were negative except for infraorbital edema (Fig. 37, *b*). His parents had noticed this, but thought it was nothing more than a facial trait peculiar to him. Although there was no real evidence that allergy was again the cause of his tense behavior, the parents agreed to proceed with allergic study. Skin tests demonstrated no definite reactions. His mother suspected that eggs upset his stomach, but elimination of this food brought about no improvement. Wheat also was negative on clinical elimination, but elimination of corn coincided with marked relief in his restlessness and irritability. On the return of corn the child had one of his worst days. He seemed unusually wild and had difficulty in going to sleep that night. Corn was withheld for a second time with the identical reaction.

In the past 3 years his parents have learned a great deal. Various friends and relatives have taken it upon themselves from time to time to experiment with his diet. It is now obvious to all that milk and corn actually must be kept from him. It has also been learned that his intolerance to corn is absolute, while his sensitivity to milk is considerably less severe. He invariably reacts to corn and pop corn, but if he has milk no oftener than twice weekly there is no apparent difficulty. His mother has been encouraged to rotate his diet so as to avoid new sensitizations.

Comment. Experience with this little boy these six years has been revealing. He demonstrates clearly that nervous manifestations of allergy are not dependent on other allergic diseases.

SUMMARY

An everyday problem in pediatric practice is the child who is restless, languid and vaguely ill and has the appearance of general ill-being without clear-cut evidence of disease. Many childhood disturbances may present this indefinite picture, and there are few more rewarding tasks than identifying these conditions. One source of disturbed behavior and vague illness is allergy, and the classic allergic behavior state constitutes a distinct syndrome which is marked by tension and fatigue with more or less evidence of constitutional allergy. Although the allergic tension-fatigue picture commonly occurs in combination with other

allergic diseases, it often occurs alone and may properly be considered a primary allergic syndrome.

REFERENCES

1. Bowen, R.: Some Practical Suggestions in the Management of Asthmatic Children. Med. Rec. & Ann., 39:1189, 1945.
2. Clarke, T. W.: The Relation of Allergy to Childhood Neuroses. J. Child Psychiatry, 1:177, 1948.
3. Clarke, T. W.: The Relation of Allergy to Character Problems in Children: A Survey. Ann Allergy, 8:175, 1950.
4. Clein, N. W.: Influence of Tonsillectomy and Adenoidectomy on Children, with Special Reference to the Allergic Implications on Respiratory Symptoms. Ann. Allergy, *10*:568, 1952.
5. Davison, H. M.: Cerebral Allergy. South. M.J., *42*:712, 1947.
6. Greenebaum, J. V., and Lurie, L. A.: Encephalitis and Behavior Disorders. J.A.M.A., *136*:923, 1948.
7. Hoobler, B. R.: Some Early Symptoms Suggesting Protein Sensitization in Infancy. Am. J. Dis. Child., *12*:129, 1916.
8. Horesh, A. J.: Allergy in Children. Clinics, 5:678, 1946.
9. Kahn, I. S.: Pollen Toxemia. J.A.M.A., 88:241, 1927.
10. Kaufman, W.: Primary Food-Induced Allergic Syndromes and Their Secondary Psychopathological Accompaniments. First International Congress of Allergists. S. Karger, Basel, Switzerland, 1952.
11. Lynch, J. D., and Snively, W. D., Jr.: Hypoproteinosis of Childhood. J.A.M.A., *147*:115, 1951.
12. May, E.: Unnatural Somnolence. Bull. et mém. soc. méd. d. hôp. de Paris, *47*: 704, 1923.
13. Piness, G.: Allergic Manifestations in Infancy and Childhood. Arch. Pediat., *42*: 557, 1925.
14. Pounders, C. M.: The Allergic Child. South. M.J., *41*:142, 1948.
15. Randolph, T. G.: Fatigue and Weakness of Allergic Origin (Allergic Toxemia) to Be Differentiated from Nervous Fatigue and Neurasthenia. Ann. Allergy, 3:418, 1945.
16. Randolph, T. G.: Allergy as a Causative Factor of Fatigue, Irritability and Behavior Problems of Children. J. Pediat., *31*:560, 1947.
17. Ratner, B.: Bone Maturation and Capillary Microscopy as Indications for the Use of Thyroid in Childhood Allergy. Ann. Allergy, *11*:419, 1953.
18. Rinkel, H. J., Randolph, T. G., and Zeller, M.: Food Allergy. Springfield, Ill., Charles C Thomas, 1951.
19. Rowe, A. H.: Allergic Toxemia Due to Food Allergy. California & West Med., 33:785, 1930.
20. Schneider, W. F.: Psychiatric Evaluation of the Hyperkinetic Child. J. Pediat., 26:559, 1945.
21. Schorer, E. H.: Idiosyncracy to Common Foods. J. Missouri Med. Soc., Dec., 1912.
22. Shannon, W. R.: Neuropathic Manifestations in Infants and Children as a Result of Anaphylactic Reactions to Foods Contained in Their Dietary. Am. J. Dis. Child., 24:89, 1922.
23. Winkelman, N. W., and Moore, M. T.: Allergy and Nervous Diseases. J. Nerv. & Ment. Dis., 93:736, 1941.

2601 Parallel Avenue
Kansas City 4, Kansas

DOSAGE IN THE TREATMENT OF POLLINOSIS

HARRY L. MUELLER, M.D.

Specific therapy in the treatment of pollinosis, as used by the great majority of allergists, is essentially the same method advanced by Noon[10] when he first described a technique of injecting graduated doses of pollen extracts as prophylactic inoculations against hay fever in 1911. Since that time there have been various controversies over the size of the doses, and the time interval between them, but aside from the introduction of perennial treatment by Brown[3] in 1932, there has been no notable change in Noon's original method.

Although it is not by any means clear as to what actually occurs when graduated doses of pollen extract are given to patients with pollinosis, it is entirely clear, after over forty years of use by many careful investigators, that the majority of patients are relieved of their symptoms in varying degree, and that during those forty years no satisfactory substitute treatment has been found. Apparently this is not a process of neutralization of the circulating pollen antigen, nor is it properly desensitization as can be done in the anaphylactic animal, but is rather a lessening of the sensitivity, partially by the production of some intermediate factor which is commonly referred to as the blocking antibody of Cooke.[5] There is not yet any proof that this is the most important factor, and there is much to suggest that some other yet unexplained mechanism of immunity is involved.

MAXIMUM TOLERATED DOSAGE*

With few exceptions, reports on the size of the dose necessary to obtain best results call for what is usually known as the maximum

* Figures given are those used by each author. For transposition from one system to another, approximate figures are: 1 cc. of 1:100 dilution extract equals 10,000 Noon units equal 20,000 P. N. units.

tolerated dose. Rackemann[12] observed early that a larger total dose does lead in most cases to a better end result and a smaller percentage of failures. Brown[4] advocated huge doses of 60,000 to 100,000 Noon units, which he stated gave such monotonously perfect results that it was unnecessary to tabulate them. In discussing results of treatment with highly purified extracts of ragweed which were electrophoretically isolated fractions, Abramson and co-workers[1] commented that in higher dosage, better protection might be provided. Shahon and co-workers[16] noted that those patients who received massive doses of pollen therapy for more than one year did well during their respective hay fever seasons. This feeling that, in general, the higher the dose the better will be the clinical results, appears time after time, in paper after paper and in the majority of textbooks. To quote only a few others, Rockwell,[15] Waldbott,[18] Black,[17] Levin,[8] Malloy[9] and Cooke[6] all subscribe in some degree to this hypothesis with various reservations.

There is general acceptance of the fact that great individual variations exist in the size of the maximum tolerated dose. Levin[8] recently published a list of six allergists whom he labeled as users of high dosage, with figures indicating maximum tolerated doses they attempted to reach, varying from 10,000 to 100,000 units. Waldbott[18] separates patients into two categories, low dose and high dose cases, and places the very sensitive patient in the former, basing this classification on strong reaction to skin testing, clinical evidence of sensitizaton to substances other than pollen, and marked local response to the individual injections. Rockwell[15] is convinced that low dosage therapy is of value in selected cases and theorizes two separate mechanisms of protection, one evoked by low dosage, the other by high dosage. Black[17] is categorical in his statement that the reaching of an adequate top dose or protective dose preseasonally is the most important of all the factors which may influence the results of pollen therapy. Although he believes that the average child, depending on age, can tolerate 15,000 to 30,000 Noon units and recommends this as a goal for top dosage, Levin[8] suggests that low dosage may be successful in areas of lower pollen count, such as the Eastern Seaboard, and agrees with Waldbott that usually the higher the degree of skin sensitivity, the lower the top dosage necessary to produce good results. Malloy[9] postulates that there is a critical level of dosage which he places at 1000 P. N. units above which one may expect to get good results and below which results are almost uniformly poor. Cooke[6] has prepared a table dividing his patients into four classes based on intensity of skin reactions, with the average dosage decreased in proportion to the increase in skin sensitivity, and with a range of top dosage from 1000 P. N. units in class A to 20,000 P. N. units in class D.

SMALL DOSAGE THERAPY

In opposition to the form of treatment which is based on the maximum tolerated dose, there is a proportionately small group of allergists who are exponents of extremely small dosage in the treatment of pollinosis. Anderson[2] was one of the early sponsors of this method, which is espoused by Hansel[7] and whose results are confirmed by Rinkel[14] and others. Hansel writes of determining the "optimum dosage," which is selected in one of three ways: (*a*) by serial dilution testing for an end point of reaction; (*b*) on the basis of severity of symptoms; or (*c*) by selecting an average dosage from a chart prepared for the purpose from previous experience. The latter is apparently the usual method selected. The average initial dosage for pollen ranges from 1:100,000 to 1:1,000,000, with the range of the optimum dosage from 1:1000 to 1:100,000,000. In severe asthma caution is given to use only 1:10,000,000,000 or 1:100,000,000,000 and for small children 1:1,000,000,000 or 1:10,000,000,000. This dosage method is used only in coseasonal treatment with pollens alone, usually intradermally, and apparently in volumes of 0.1 cc. or less. How this is used in combination with other allergens, when multiple sensitivity occurs, is not entirely clear. The interval between injections for pollen is said to be from a matter of hours to three or four days.

Hansel states that after the initial dose, subsequent doses remain the same or are either increased or decreased according to the response. Increase of dose should follow if relief lasts only two to three days, and yet if there is no response at all, the dose should be decreased. It would seem that this resolves itself into an infallible formula, for if the patient is doing well in the most recent interval between injections, the correct dose must have been given and should be repeated at the next visit; but if the patient is doing poorly in the interval, then the dose must have been wrong and must be increased or decreased at the subsequent visits until the patient does well again. If the reader finds this hard to follow, he is referred to Hansel's text[7] for greater detail.

An intermediate dosage schedule is followed by Ratner,[13] who describes a method whereby he uses a single dilution of 1:5000 in amounts of 0.1 to 0.3 cc. for all patients and gives these injections in varying intervals from hours to several months. Two minims of epinephrine 1:1000 solution are given in the syringe with pollen mixtures. Each subsequent dose is considered a booster to an established immunity. One marvels at the simplicity to which such a standardization would reduce the treatment of pollinosis with its tremendous individual differences in degree of sensitivity, but one also wonders why the variation of 0.1 to 0.3 cc. is not further simplified by the choice of a single decimal.

Although there are exceptions in the treatment of pollinosis, one

statement can be made concerning the present use of pollen therapy, namely, that it is generally effective in the hands of most allergists. With minor variations the degree of effectiveness seems to be about equal regardless of the method used; and if we are to accept the reports of various investigators, equally good results seem to be obtainable regardless of the dosage used.

It is not hard to accept the equally good results obtained by using any one of the three generally accepted methods of treatment; that is, preseasonal, coseasonal and perennial, since these are basically dependent on the same theory of hyposensitization, being variations in technique and timing to fit the patients and the season. However, it is difficult to understand how results can be equally successful when the dosage may range from solutions of 1:50 to solutions of 1:10,000,000,000 in the same type of patient. In order to comprehend the difference in such dosage it is comparable to a solution of 1 ounce of water in which one 5-grain aspirin tablet has been dissolved, to a solution of 1 ounce of water from the combined amount contained in twenty-five average-sized swimming pools in which one 5-grain aspirin tablet has been dissolved. Or put another way, since 1 cc. of a 1:1,000,000 solution contains 1 Noon pollen unit, which is equal to about five pollen grains, when one gets to a dilution of 1:10,000,000,000, it results in 1 cc. containing 1/2000 of a pollen grain. This would be about 1,000,000 molecules, somewhat less than the billion billion gas molecules per cubic centimeter to be found in an ordinary vacuum at one atmosphere and zero degrees centigrade. To call solutions of 1:1,000,000,000 "small dosage" would seem to be something of an understatement. As Glaser* once remarked, referring to one of the leading proponents of the low dosage regimen, "The solutions he now advocates are so dilute that one wonders why, instead of giving an injection, he doesn't merely walk past the patient holding the syringe in his hand."

RECOMMENDED DOSAGE

Rockwell[15] said that if the treatment of pollinosis is to succeed, it must be specific, and therefore a correct and complete etiologic diagnosis must be made. We would agree completely with this precept, and the following general outline of therapy has been used for a number of years at the Children's Medical Center with what is considered good results.

Though the extremely low dosage discussed earlier would seem to be innocuous, at the best, we also believe that the high dosage advocated by Levin,[8] Brown[4] and others is likewise extreme and unnecessary for the attainment of satisfactory results. Consequently our treatment strives

* Pediatric Luncheon Round Table, American College of Allergists, Pittsburgh, 1952.

to follow the concept of maximum tolerated dosage within the bounds of comfort and safety for the patients.

Except in rare selected cases for preseasonal treatment, perennial treatment is used as the method of choice. Coseasonal treatment with its frequent visits does not readily adapt itself to our clinic schedule. Although the patients may present themselves for the first time during their season, children do not demand immediate relief, nor do the exigencies of breadwinning or housekeeping give cause for that demand as they do in adults.

In some instances patients have been started on treatment just before or during the pollen season, in the usual manner, and have reported beneficial results. It would therefore not seem necessary to defer treatment until the next pollen season in these patients.

The initial dose is based on the degree of skin sensitivity and the severity of symptoms. In general, children are not so sensitive as adults and tolerate pollen injections well. Most children over four years of age can be started on a dose of 0.1 cc. of 1:10,000 dilution and will reach a top dose of 0.3 cc. of 1:100 dilution. Every patient, however, is a law unto himself, and in some it may be necessary to start with a smaller initial dose and reach a smaller top dose.

Subcutaneous injections are given every four to seven days and increased according to Table 34. It has been said that the maximum period of seven days between increasing doses was established because Noon's original clinic met once a week. There is some indication that this is an arbitrary figure which can be increased, but until this is firmly established as a safe procedure, the seven day interval had best be followed. If the local reaction as characterized by redness or swelling is as large as a silver dollar or, although smaller, lasts more than twenty-four hours, the dose is not increased at the next visit. If this local reaction remains the same after three successive injections, it is an indication that tolerance has been reached, and the dose is dropped one step and then continued as the optimum top dose for that patient. If there are any signs of a beginning general reaction such as itching, sneezing, cough, hives or a feeling of tightness, 0.3 cc. of a 1:100 solution of epinephrine is given immediately. After any general reaction, no matter how slight, the next dose is at least cut in half, and reduced more if the reaction is severe. If a general reaction occurs early in the treatment with the weaker solutions, another attempt is made to increase the dose again, progressing by half steps on the dosage table. If a general reaction occurs later in the treatment with the strongest solution, the dose is cut back as described. This is considered the optimum top dose, and no further attempt is made to increase the dosage.

After each injection the patient remains under observation for twenty

minutes and is checked for local or systemic reactions before being released. The parent is instructed to watch for any appearance or change of local reaction and/or systemic symptoms in the period between injections.

Once the optimum top dose is reached, it is given once every four weeks up to the start of the pollen season. During the pollen season the dose is cut in half and then built up again some time between the end of the pollen season and the start of the next season. If for any reason the interval between doses is more than four weeks, the next dose is proportionately reduced.

TABLE 34. *Average Pollen Dosage for Children*

1:10,000	1:1000	1:100
0.10 cc.	0.05 cc.	0.05 cc.
0.20 cc.	0.10 cc.	0.075 cc.
0.30 cc.	0.20 cc.	0.10 cc.
0.50 cc.	0.30 cc.	0.15 cc.
	0.50 cc.	0.20 cc.
		0.30 cc.
		0.40 cc.
		0.50 cc.
		0.60 cc.

This is a good, safe general rule for the clinic or routine office practice. In selected, carefully observed patients the interval has been increased to five or six weeks with no difficulty in toleration; similarly, patients have been carried through the pollen season without reducing the dosage and without reactions. As yet not enough experience has been had to recommend this for general use, but the advantages to the patient in convenience and expense are obvious.

Certain precautions should be emphasized. Some patients who give little or no reaction to skin tests may be very sensitive and will not tolerate as high a top dose as many patients who react strongly to skin tests. Occasional patients, after reaching their optimum top dose, will not tolerate an interval of four weeks either because they have too much reaction at that interval or have return of symptoms before that time has elapsed. These patients must be put on a two or three week schedule. Regardless of the absence of local or general reactions, a top dose exceeding 0.6 cc. of 1:100 dilution is not advised, nor do we believe that a larger dose is necessary to obtain good clinical results except in rare instances.

Results

The treatment of pollinosis in many children over a period of years has resulted in a number of general observations. (1) Pollinosis without

other sensitivities is not common in children before the age of puberty. (2) Good clinical results are obtained in over 80 per cent of patients by these methods. (3) Highly sensitive patients as measured by skin testing by and large have a higher percentage of good results than those with very little sensitivity, provided the dosage is kept proportionately small. (4) Contrary to general reports, many of our treated hay fever patients, concurrent with treatment or subsequently, do get asthma. (5) Frequently, after several years' treatment tolerance decreases and the top dose may have to be decreased. (6) Those with the best clinical results are more apt to be able to stop treatment successfully after three years. (7) Interpretation of results is extremely difficult in view of the large number of variables present.

Unlike many other conditions, there are no exact criteria in allergy, measurable in any way, for judging results. In fact the only reaction in allergy that can be measured, according to Rackemann,[11] is the level of absolute tolerance, and this is not necessarily parallel to other measurements of sensitivity, nor is it constant from year to year.

Consequently, with diagnosis that is difficult, with multiple antigens, with patients who may be sensitive to different fractions of these antigens and have varying levels of sensitivity to these fractions, with antigens from varying sources that may have varying degrees of antigenicity, with differences in the strength of extracts and with differences in pollen seasons, *is it any wonder that when that greatest variable, the patients', the parents' or the doctors' interpretation, is added, judging of results is a far from accurate procedure?*

REFERENCES

1. Abramson, H. A., Loebl, M., Gettner, H. H., and Sklarofsky, B.: Therapy of Ragweed Hay Fever with Electrophoretically Isolated Fractions. Ann. Allergy, 8:594, 1950.
2. Anderson, J. M.: Small Dosage Treatment of Hay Fever. J. Allergy, 3:306, 1932.
3. Brown, A.: The Perennial Treatment of Seasonal Hay Fever. J. Allergy, 3:113, 1932.
4. Brown, G. T.: Maximum Dosage in Pollen Therapy. J. Allergy, 3:180, 1932.
5. Cooke, R. A.: Allergy in Theory and Practice. Philadelphia, W. B. Saunders Company, 1947, pp. 57–67.
6. Cooke, R. A.: Op. cit., pp. 197–198.
7. Hansel, F. K.: Clinical Allergy. St. Louis, C. V. Mosby Company, 1953, pp. 516–519, 745–752.
8. Levin, S. J.: The Optimum Dose of Pollen in the Treatment of Pollinosis of Children. J. Pediat., *41*:294, 1952.
9. Malloy, C. J.: The Treatment of Ragweed Hay Fever. Canad. M.A.J., *68*:583, 1953.
10. Noon, L.: Prophylactic Inoculations against Hay Fever. Lancet, *1*:1572, 1911.
11. Rackemann, F. M.: Pollen Tolerance; Its Bearing on the Treatment of Hay Fever. J. Allergy, *18*:164, 1947.

12. Rackemann, F. M., Graham, L. B., and Scully, M. A.: The Optimal Dosage in the Treatment of Hay Fever. J. Immunol., *11*:91, 1926.
13. Ratner, B.: Management of Hay Fever in Children, with Special Emphasis on Immunization. J. Pediat., 39:102, 1951.
14. Rinkel, H. J.: Inhalant Allergy. Ann. Allergy, 7:625, 1949.
15. Rockwell, G. E.: Hay Fever. A Review of the Literature for 1945. Ann. Allergy, 4:148, 1946.
16. Shahon, H. I., Lappin, H., Agranat, V., Kamberg, I., and Parish, F. A.: Injections of Massive Doses of Pollen Extract at Three-Week Intervals and Their Effect on Skin Test Sensitivity. Ann. Allergy, 9:77, 1951.
17. Vaughan, W. T., revised by Black, J. H.: Practice of Allergy. 2d ed. St. Louis, C. V. Mosby Company, 1948, p. 657.
18. Waldbott, G. L.: Pollen Infections during the Hay Fever Season. GP, 2:49, 1950.

31 Church Street
Winchester, Mass.

INDEX OF AUTHORS

Abelson, Neva M., *Aug.*, 541
Alway, Robert H., *Nov.*, 757, 901
Arena, Jay M., *Nov.*, 771

Baffes, Thomas G., *Aug.*, 709
Bakwin, Ruth Morris, *Nov.*, 921
Batson, Blair, *May*, 349
Bruns, Paul D., *Nov.*, 845

Cassels, Donald E., *Feb.*, 251
Chisholm, Tague C., *Nov.*, 907
Christian, Joseph R., *Aug.*, 555
Christie, Amos, *May*, 349
Clagett, O. Theron, *Feb.*, 173
Clein, Norman W., *Nov.*, 949
Cole, Wyman C. C., *Aug.*, 527
Cooke, Robert E., *Aug.*, 649
Crawford, W. L., *Aug.*, 639
Crump, Jean, *Nov.*, 987

Dees, Susan C., *Nov.*, 1017
Denton, Robert, *Aug.*, 625
Dietrich, Harry F., *Nov.*, 759
DuShane, James W., *Feb.*, 115, 173

Edwards, Jesse E., *Feb.*, 13
Eiben, Robert M., *May*, 405
Etteldorf, James N., *Aug.*, 593

Fell, Egbert H., *Feb.*, 197
Forney, Richard A., *Feb.*, 197
Fries, Joseph H., *Nov.*, 995

Gaffney, Paul C., *May*, 283
Gasul, Benjamin M., *Feb.*, 131
Gibson, Stanley, *Feb.*, 1, 3
Girdany, Bertram R., *May*, 303
Glaser, Jerome, *Nov.*, 919

Harrison, Harold E., *May*, 335
Hess, Julius H., *Aug.*, 679
Holinger, Paul H., *Nov.*, 827
Hughes, James G., *May*, 447

Johnson, Frank R., *Feb.*, 235
Johnston, Kenneth C., *Nov.*, 827
Johnstone, Douglas E., *Nov.*, 1007

Keith, John D., *Feb.*, 73
Klein, Robert, *May*, 321

Landauer, Kenneth S., *May*, 483
Langendorf, Richard, *Feb.*, 215
Levin, Samuel J., *Nov.*, 975
Livingston, Samuel, *Nov.*, 801
Logan, George B., *Nov.*, 811

McOsker, Thomas C., *Nov.*, 787
McQuiston, William O., *Feb.*, 147
Marienfeld, Carl J., *Feb.*, 131
Matheson, A., *Nov.*, 929
Miller, Robert A., *Feb.*, 51
Mitchell, F. Thomas, *Aug.*, 513
Mueller, Harry L., *Nov.*, 1039

Nadas, Alexander S., *Nov.*, 859
Nelson, Lloyd S., *Nov.*, 963
Nicholson, Ruth L., *Aug.*, 661
Nitzke, Everett A., *Aug.*, 685

Olshaker, Bennett, *Aug.*, 722
Overall, James C., *Nov.*, 969

Pick, Alfred, *Feb.*, 215
Pickering, Donald E., *Nov.*, 873
Pickles, Wilfred, *Nov.*, 787
Potter, Edith L., *Aug.*, 515
Potts, Willis J., *Feb.*, 1, 159; *Aug.*, 709

Rammelkamp, Charles H., Jr., *Feb.*, 265
Ratner, Bret, *Nov.*, 943
Riker, William L., *Feb.*, 181
Robbins, Frederick C., *May*, 405

Sanford, Heyworth N., *Aug.*, 573
Shaffer, Thomas E., *May*, 421
Shwachman, Harry, *May*, 389
Sieber, William K., *May*, 303
Smith, Nathan J., *May*, 367
Spears, Ethel M., *May*, 483
Speer, Frederic, *Nov.*, 1029
Spencer, Bernard J., *Nov.*, 907
Stevenson, Stuart Shelton, *May*, 281, 433
Stoesser, Albert V., *Nov.*, 963
Stolzer, Bertrand L., *Feb.*, 265
Stuart, Harold C., *May*, 467
Szewczyk, Thaddeus S., *Aug.*, 607

Taylor, E. Stewart, *Aug.*, 587

Tompkins, Winslow S., *Aug.*, 687
Tuttle, Arliss H., *Aug.*, 593

Vaughan, Victor C., III, *May*, 367
Vignec, Alfred J., *Aug.*, 661

Wickster, George Z., *Aug.*, 555
Wiehl, Dorothy G., *Aug.*, 687
Winters, Robert W., *Nov.*, 873
Wyatt, Oswald S., *Nov.*, 907

Ziegler, Robert F., *Feb.*, 93

INDEX TO VOLUME I (1954)

Page numbers of clinic and symposium titles are given in **boldface** type.

ABDOMEN, pain in, in gastrointestinal allergy, *Nov.*, 998
Abnormalities. See also under specific organs and regions, as *Heart*; *Liver*; etc.
  congenital, as cause of retarded growth, *May*, 439
    effect on premature mortality, *Aug.*, 576
  fatal, effect on prematurity, *Aug.*, 518
Abruptio placentae, *Aug.*, 555
Accident(s), and emergencies, symposium on, *Nov.*, **757–918**
  check list against, *May*, 430
  motor vehicle, deaths from, table, *Nov.*, 760
  parent-child relationship, *May*, 429
  prevention, *May*, **421–432**; *Nov.*, **759–769**
    in infancy, *Nov.*, 763
    in toddlers, *Nov.*, 764
  protection versus education, *May*, 427
  repeaters, *May*, 428
  risks and precautions at various age levels, table, *May*, 426
  types, *May*, 422
Accident-proneness, *May*, 430
  in toddlers, *Nov.*, 767
Acetylcholine bromide in paroxysmal tachycardia, *Feb.*, 225
Achievement, emotional need of children for, *May*, 458
Achiness in allergic tension-fatigue syndrome, *Nov.*, 1031
Achromycin hydrochloride in laryngotracheobronchitis, *Nov.*, 815
Acid, acetylsalicylic, in rheumatic fever, acute, *Feb.*, 269
  ascorbic, for premature infant, *Aug.*, 671
  boric, poisoning by, *Nov.*, 783
  para-aminosalicylic, in tuberculous meningitis, *May*, 415
Acid-base equilibrium, disturbances of, *Nov.*, 892
    physiologic background, *Nov.*, 892
Acidosis, diabetic. See *Diabetic acidosis*.
  metabolic, *Nov.*, 894
  respiratory, *Nov.*, 894
  severe, and circulatory collapse with rapid response to therapy, *May*, 344
ACTH, in asthma, acute, *Nov.*, 981
    table, *Nov.*, 820
  in congestive failure, acute, *Nov.*, 869
  in dermatitis, atopic, *Nov.*, **969–974**
      dosage, *Nov.*, 971
      principles, *Nov.*, 870
  in infectious diseases, *May*, 419
  in rheumatic fever, acute, *Feb.*, 271
  in status asthmaticus, *Nov.*, 984
Adams-Stokes attack. See *Heart, block*.
Adolescence, nutritional problems, *May*, 478
  obesity in, *May*, 479
  problems associated with early and late maturing, *May*, 476
  problems requiring medical attention, *May*, 476
Adolescent, The, *May*, **467–481**
Adrenal(s), aplasia, in newborn, *May*, 331
  hemorrhage, in newborn, *May*, 331
  hyperplasia, in newborn, *May*, 331
  hypofunction, persistent, in newborn, *May*, 331
    transient, in newborn, *May*, 329
  hypoplasia, in newborn, *May*, 331
  insufficiency, in premature infant, *Aug.*, 646, 674
  physiology, neonatal, *May*, **321–334**
      clinical correlations, *May*, 329
Aerosol solutions, *Aug.*, 633
Aerosol therapy, background and techniques, *Aug.*, 626
Affection, emotional need of children, for, *May*, 457
Agammaglobulinemia, treatment with immune substances, *May*, 418
Air and food passages, foreign bodies in, *Nov.*, **827–843**. See also *Foreign bodies*.
Airway. See *Respiratory system*.

Alkali, caustic, poisoning by, *Nov.*, 773
Alkalosis, metabolic *Nov.*, 895
respiratory, *Nov.*, 894
Allergic. See also *Allergy.*
Allergic celiac syndrome, *Nov.*, **1007–1016**
clinical criteria, *Nov.*, 1009
diagnosis, *Nov.*, 1008
differential diagnosis, *Nov.*, 1013
laboratory criteria, *Nov.*, 1010
treatment, *Nov.*, 1014
Allergic children, psychosomatics in, essentials of, *Nov.*, **921–928**
Allergic convulsive disorders, *Nov.*, 1019
Allergic cough, *Nov.*, 988
Allergic epilepsy, *Nov.*, 1020
Allergic headaches, *Nov.*, 1018
Allergic respiratory conditions, vaccine treatment, value of, *Nov.*, **987–993**
Allergic tension-fatigue syndrome, *Nov.*, **1029–1037**
clinical picture, *Nov.*, 1030
differential diagnosis, *Nov.*, 1032
physical findings, *Nov.*, 1032
Allergy, children with, general management, *Nov.*, **943–948**
contact factors, *Nov.*, 960
gastrointestinal, diagnosis, *Nov.*, 1000
etiology, *Nov.*, 996
in children, manifestations, *Nov.*, **995–1005**
incidence, *Nov.*, 995
laboratory investigations, *Nov.*, 1004
mechanism, *Nov.*, 996
nutrition and, *Nov.*, 999
protective mechanisms, *Nov.*, **997**
roentgen findings, *Nov.*, 1002
symptoms, *Nov.*, 997
treatment, *Nov.*, 1004
history in, *Nov.*, 944
inhalant factors, *Nov.*, 960
meningeal, *Nov.*, 1023
milk, cow's, in infants, *Nov.*, **949–962**. See also *Milk allergy.*
nasal, *Nov.*, 988
neuritic, *Nov.*, 1023
neurologic, diagnosis, *Nov.*, 1017
in childhood, *Nov.*, **1017–1027**
protein skin tests for, *Nov.*, 946
respiratory, *Nov.*, 987
vaccine treatment, dosage, *Nov.*, 990
technique, *Nov.*, 990
skin tests in, value of, *Nov.*, **929–942**. See also *Skin tests.*
symposium on, *Nov.*, **919–1046**
to foods, *Nov.*, 960
treatment, *Nov.*, 947
aim of, *Nov.*, 927
Alternating positive-negative pressure, *Nov.*, 852
Aminophylline in asthma, *Nov.*, 818, 980
in status asthmaticus, *Nov.*, 984
Analeptics as cause of respiratory difficulty in newborn, *Nov.*, 854
Anaglesia, as cause of respiratory difficulty in newborn, *Nov.*, 853
in relation to blood oxygen saturation, *Aug.*, 588
in premature infants, *Aug.*, 589
Anemia(s), aplastic, *May*, 372
as cause of retarded growth, *May*, 443
Cooley's. See *Thalassemia.*
due to deficiency in antipernicious anemia factor. See *Anemia, megaloblastic.*
due to excessive destruction of erythrocytes, *May*, 381
due to excessive loss of erythrocytes, *May*, 380
due to inadequate erythrocyte or hemoglobin production, *May*, 370
hemolytic, due to congential abnormalities in production of hemoglobin or erythrocytes, *May*, 383
in premature infant, *Aug.*, 600
hypochromic, in differential diagnosis of rheumatic fever, *Feb.*, 260
hypoplastic, congenital, *May*, 372
in erythroblastotic premature infant, *Aug.*, 544
in premature infants, *Aug.*, **593–606**
table, *Aug.*, 595
Mediterranean. See *Thalassemia.*
megaloblastic, *May*, 378
of infancy, *May*, 379
of blood loss in premature infant, *Aug.*, 601
of infancy and childhood, *May*, **367–388**
classification, *May*, 370
of iron deficiency, *May*, 373
and diarrhea in infant, *May*, 345
diagnosis, *May*, 375
symptoms, *May*, 375
treatment, *May*, 376
pathologic, in premature infant, *Aug.*, 600
pernicious, *May*, 377
physiologic, in premature infants, *Aug.*, 596
prophylaxis, *Aug.*, 598
treatment, *Aug.*, 598
premature labor and, *Aug.*, 706
Anesthesia, as cause of respiratory difficulty in newborn, *Nov.*, 853
for cardiac surgery, *Feb.*, **147–157**
for surgical treatment of patent ductus arteriosus, *Feb.*, 165
in relation to blood oxygen saturation, *Aug.*, 588
in premature infants, *Aug.*, 589
Aneurysm, of aortic sinus, pathology, *Feb.*, 19
pulmonary, arteriovenous, diagnosis, *Feb.*, 145
Angiocardiography, *Feb.*, **73–92**

Angiocdema as symptom of milk allergy in infants, *Nov.*, 957
Angiogram, venous, technique, *Feb.*, 74
Aniline dyes, poisoning by, *Nov.*, 780
Anomalies. See *Abnormalities.*
Anorexia as symptom of milk allergy in infants, *Nov.*, 957
Anoxic spells, *Nov.*, 865
prognosis, *Nov.*, 867
Antibiotics, dosage ranges, table, *May*, 408
in acute asthma, *Nov.*, 981
in status asthmaticus, *Nov.*, 984
types, routes and dosages, table, *Aug.*, 674
Antidote, universal, for poisoning, *Nov.*, 783
Antihistaminics in acute asthma, *Nov.*, 980
Antipruritics in chronic atopic dermatitis, *Nov.*, 968
Antipyrine in croup, *Nov.*, 813
Antistreptolysin O titer in diagnosis of rheumatic fever, *Feb.*, 261
Antitoxin, diphtheria, dosage, *Nov.*, 816, 817
Anus, atresia, in newborn, *May*, 318
in premature infant, *Aug.*, 578
imperforate, with or without fistulas, *Nov.*, 915
stenosis, in premature infant, *Aug.*, 578
Aorta, ascending, atresia or marked hypoplasia, with or without mitral atresia or stenosis, diagnosis, *Feb.*, 144
coarctation, and patent ductus arteriosus, pathology, *Feb.*, 17
aortography in, *Feb.*, 90
catheterization in, *Feb.*, 101
diagnosis, *Feb.*, 120, 174
and management, *Feb.*, **173–180**
electrocardiogram in differential diagnosis, *Feb.*, 65
in newborn premature, *Aug.*, 580
pathology, *Feb.*, 16
Aortagram, technique, *Feb.*, 75
Aortic arch, anomalies, and treatment, *Feb.*, **181–195**
diagnosis, *Feb.*, 187
prognosis, *Feb.*, 191
double, in newborn premature, *Aug.*, 579
Aortic septum, defect of, pathology, *Feb.*, 17
Aortic sinus, aneurysm of, pathology, *Feb.*, 19
Aortic valve, atresia, pathology, *Feb.*, 40
murmurs, *Feb.*, 9
stenosis, diagnosis, *Feb.*, 122
pathology, *Feb.*, 19
Aorticopulmonary fistula, pathology, *Feb.*, 17
Aortography, *Feb.*, 88
Appearance, general, in poliomyelitis, *May*, 486
Appetite in celiac syndrome and mucoviscidosis, *May*, 396
Arrhythmias, cardiac, *Feb.*, **215–234**
complicating cardiac surgery, *Feb.*, 153
extrasystoles, *Feb.*, 258
in diagnosis of rheumatic fever, *Feb.*, 257
Arteries, coronary, anomalous origin from pulmonary artery, diagnosis, *Feb.*, 124
left, aberrant, originating from pulmonary artery, *Feb.*, 236, 237
anomalous origin, electrocardiographic patterns, *Feb.*, 61, 62
from pulmonary trunk, pathology, *Feb.*, 21
Ascorbic acid. See *Acid.*
Asphyxia, causes, *Aug.*, 532
in premature infant, *Aug.*, 580
Asphyxial states, *Nov.*, 823
Aspiration of newborn, methods, *Nov.*, 846
Aspirin. See *Acid, acetylsalicylic.*
Asthma, *Nov.*, 817, 989
as symptom of milk allergy in infants, *Nov.*, 957
history-taking, *Nov.*, 923
management, *Nov.*, 925, **975–985**
personality and, *Nov.*, 924
physical factors, *Nov.*, 925
psychologic factors, *Nov.*, 921
Asthmatic attack, acute, management in childhood, *Nov.*, **975–985**
Asthmatic child, *Nov.*, 921
need for psychiatrist, *Nov.*, 926
psychologic approach, *Nov.*, 923
Ataxia, Friedreich's, *Feb.*, 260
Atelectasis, in premature infant, *Aug.*, 581
pulmonary resection for, *Aug.*, 717
Atmosphere, supersaturated, influence on fluid balance, *Aug.*, 635
Atopic dermatitis, local treatment, *Nov.*, **963–968**. See also *Dermatitis, atopic.*
Atrial fibrillation, *Feb.*, 219
Atrial flutter, *Feb.*, 219, 222
Atrial septum, defect of, and intact ventricular septum, with pulmonary valvular stenosis, pathology, *Feb.*, 33
and mitral stenosis, pathology, *Feb.*, 27
angiocardiography in, *Feb.*, 88
diagnosis, *Feb.*, 124
lower, defect of, and deformity of atrioventricular valves, pathology, *Feb.*, 28
murmurs, *Feb.*, 11
Atrioventricular canal, common, persistent, pathology, *Feb.*, 28
Atrioventricular dissociation without block, *Feb.*, 218

Atrioventricular valves, deformity of, and defect of lower atrial septum, pathology, *Feb.*, 28
Atrioventricularis communis, angiocardiography in, *Feb.*, 86
Atrium, left, anomalous connection with persistent left superior vena cava, pathology, *Feb.*, 48
communication with coronary sinus, pathology, *Feb.*, 29
enlargement of, fluoroscopic and roentgenographic findings, *Feb.*, 137
right, enlargement of, fluoroscopic and roentgenographic findings, *Feb.*, 136
Atropine poisoning, *Nov.*, 777
Aureomycin in acute asthma, *Nov.*, 981
Authority, emotional need of children for, *May*, 459
Autonomous premature unit, *Aug.*, **661–678**. See also *Premature unit*.
Avertin in convulsive seizures, *Nov.*, 809

BAL in treatment of poisoning, *Nov.*, 784
BCG. See *Tuberculosis, immunization*.
Barbiturate intoxication, *Nov.*, 775
Bedpans, care and use for poliomyelitis patients, *May*, 489
Behavior problems, conferences, *May*, 455
evaluation, basic information, *May*, 457
scope of, *May*, 456
examination of child, *May*, 454
first conference, arranging, *May*, 450
circumstances, *May*, 451
initial contact with problem, *May*, 449
practical approach to, *May*, **447–466**
summing up the problem, *May*, 456
tests and laboratory procedures, *May*, 454
treatment, general approach, *May*, 456
Belladonna poisoning, *Nov.*, 777
Benadryl in acute asthma, *Nov.*, 980
Benzine poisoning, *Nov.*, 774
Bicillin, in acute asthma, *Nov.*, 981
in rheumatic fever, recurrent, prophylaxis, *Feb.*, 273
Biliary tract, anomalies, in newborn premature, *Aug.*, 579
Birth weight, *Aug.*, 699
average, of babies born to standard and underweight mothers, table, *Aug.*, 693
in relation to dietary supplement, table, *Aug.*, 703
relative to body build in relation to dietary supplement, *Aug.*, 704
Births, live, and neonatal mortality, table, *Aug.*, 517
Blood, circulation, collapse, and severe acidosis with rapid response to therapy, *May*, 344
venous, pulmonary, impaired, pathology, *Feb.*, 22
examinations, in convulsions, *Nov.*, 804
flow. See *Blood, circulation*.
oxygen saturation, anesthesia or analgesia in relation to, *Aug.*, 588
oxygen studies in premature, *Aug.*, **587–591**
sedimentation rate in diagnosis of rheumatic fever, *Feb.*, 260
transfusion, exchange, equipment for, *May*, 296
general considerations, *May*, 300
in erythroblastosis fetalis, *May*, 295
in premature infant, *Aug.*, 543
indications, *May*, 294
place and personnel, *May*, 296
postexchange care, *May*, 299
technique, *May*, 297
history, in hemolytic disease of newborn, *May*, 289
in erythroblastosis fetalis, effects of, *May*, 294
in premature infants, *Aug.*, 583, 646, 675
type, in hemolytic disease of newborn, *May*, 289
whole, in diarrhea in infancy, *May*, 340
Blood plasma in diarrhea in infancy, *May*, 340
Blood vessels, transposition, angiocardiography in, *Feb.*, 81
complete, diagnosis, *Feb.*, 141
pathology, *Feb.*, 42
surgical treatment, *Feb.*, 210
vascular ring, in newborn, *May*, 307
Bone marrow hypofunction in premature infant, *Aug.*, 603
Boric acid poisoning, *Nov.*, 783
Braces in poliomyelitis, adjustment of, *May*, 500
Bradycardia, sinus, *Feb.*, 215, 218
Brain, concussion, treatment, *Nov.*, 790
congestion, treatment, *Nov.*, 790
contusion, treatment, *Nov.*, 791
edema of, acute, treatment, *Nov.*, 794
Breasts, development in adolescence, *May*, 475
Bronchi, obstruction of, *Nov.*, 817
Bronchiectasis, pulmonary resection for, *Aug.*, 711
Bronchiolitis, acute, *Nov.*, 816
Bronchitis, capillary, *Nov.*, 816
terminal, acute, *Nov.*, 816
Bronchodilators in acute asthma, *Nov.*, 979

Bronchoscopy in status asthmaticus, *Nov.*, 984
Burns, prevention, in toddlers, *Nov.*, **765**
thermal, estimation of severity, *Nov.*, 901
in children, management of acute phase, *Nov.*, **901–906**
phase I, *Nov.*, 902
phase II, *Nov.*, 903
phase III, *Nov.*, 903
severe, natural history, *Nov.*, 902
treatment, *Nov.*, 903
local, *Nov.*, 905
Burow's solution in acute exudative eczema, *Nov.*, 965

Caffergone in migraine, *Nov.*, 1019
Calories in fluid and electrolyte maintenance therapy, *Nov.*, 876
Camphor poisoning, *Nov.*, 778
Camphorated oil, poisoning, *Nov.*, 778
Cardiac emergencies, *Nov.*, **859–871**
Cardio-esophageal relaxation. See *Esophagus, chalasia.*
Cardiovascular anomalies, congenital, cyanotic, surgical treatment, *Feb.*, **197–213**
with decreased pulmonary blood flow, *Feb.*, 200
with normal or increased pulmonary blood flow, *Feb.*, 210
Cardiovascular diseases, symposium on, *Feb.*, **1–274**
Cardiovascular system, congenital malformations, effect on premature mortality, *Aug.*, 579
Catheterization, cardiac, clinical, *Feb.*, **93–113**. See also *Heart, catheterization.*
Celiac crises, *May*, 397
Celiac disease, idiopathic, vs. allergic celiac syndrome, *Nov.*, 1013
Celiac syndrome, *May*, 389
allergic, *Nov.*, **1007–1016**. See also *Allergic celiac syndrome.*
and mucoviscidosis, *May*, **389–403**
bacteriologic studies, *May*, 400
clinical variants, *May*, 402
diagnosis, *May*, 390
differential diagnosis, *May*, 392
laboratory investigation, *May*, 398
newer concepts, *Nov.*, 1007
onset, age at, *May*, 395
prognosis, *May*, 402
symptoms and signs, *May*, 395
treatment, *May*, 401
Cerebrospinal fluid examinations in convulsions, *Nov.*, 805
Cesarean section, incision into placental or umbilical blood vessels at, *Aug.*, 559
Chalasia of esophagus in newborn, *May*, 307
Chemotherapy, agents, dosage ranges, table, *May*, 408
in acute asthma, *Nov.*, 981
in status asthmaticus, *Nov.*, 984
Chest. See *Thorax.*
Childhood, accident prevention in, *Nov.*, **759–769**. See also *Accident(s), prevention.*
anemias of, *May*, **367–388**
Chloral hydrate, in atopic dermatitis, chronic, *Nov.*, 968
in convulsive seizures, *Nov.*, 809
Chlor-Trimeton in acute asthma, *Nov.*, 980
Chloramphenicol in meningitis, *May*, 413
Chloromycetin. See *Chloramphenicol.*
Choking as symptom of milk allergy in infants, *Nov.*, 955
Chorea, fidgets and tics, *Feb.*, 259
Sydenham's, *Feb.*, 259
Clinical advances, symposium on, *May*, **281–481**
Coal tar, crude, in chronic eczema, *Nov.*, 967
Coarctation of aorta. See under *Aorta.*
Colds, chest, as symptom of milk allergy in infants, *Nov.*, 955
nose, as symptom of milk allergy, *Nov.*, 956
Colic as symptom of milk allergy in infants, *Nov.*, 954
Colon, achalasia. See *Megacolon, congenital.*
Concussion of brain, treatment, *Nov.*, 790
Constipation as symptom of milk allergy in infants, *Nov.*, 956
Convulsion, febrile, simple, *Nov.*, 801
history in, *Nov.*, 803
isolated, management of, *Nov.*, **801–810**
termination of attack, *Nov.*, 807
treatment, *Nov.*, 806
laboratory procedures, *Nov.*, 804
physical examination, *Nov.*, 804
Convulsive disorders, allergic, *Nov.*, 1019
treatment, results of, table, *Nov.*, 1021
Convulsive seizures, disorders associated with, *Nov.*, 801
table, *Nov.*, 802
Cooley's anemia. See *Thalassemia.*
Cooling of body for cardiac surgery, *Feb.*, 154
Cor biloculare, pathology, *Feb.*, 38
Cor triatriatum, pathology, *Feb.*, 27
Cor triloculare biatriatum, pathology, *Feb.*, 38
Corticosteroids, physiology, in newborn, *May*, 322
Corticotropin. See *ACTH.*
Cortisone, in asthma, acute, *Nov.*, 981
table, *Nov.*, 820
in congestive failure, acute, *Nov.*, 869
in dermatitis, atopic, *Nov.*, **969–974**

Cortisone, in dermatitis, atopic, dosage, *Nov.*, 971
principles, *Nov.*, 970
in infectious diseases, *May*, 419
in rheumatic fever, acute, *Feb.*, 269
in status asthmaticus, *Nov.*, 984
Cough, allergic, *Nov.*, 988
as symptom of milk allergy in infants, *Nov.*, 955
Cough medicine in acute asthma, *Nov.*, 977
Cow's milk allergy in infants, *Nov.*, **949–962**. See also *Milk allergy*.
Croup, *Nov.*, 813
as symptom of milk allergy in infants, *Nov.*, 955
Crown-sole length, average, of babies born to standard and underweight mothers, table, *Aug.*, 693
Cyanosis, in diagnosis of heart disease, *Feb.*, 4, 6
of cardiac origin, *Feb.*, 132
persistent, in congenital heart disease, pathology, *Feb.*, 32
with absent right ventricle or no right ventricular hypertrophy, *Feb.*, 46
Cytomegalic inclusion disease in premature infant, *Aug.*, 601

DDT poisoning, *Nov.*, 780
DEBD. See *Dipenicillin G*.
Death(s), neonatal, *Aug.*, 522
sudden, *Nov.*, 821
Decapryn in acute asthma, *Nov.*, 980
Defecation, pattern of, normal, *Nov.*, 912
Deficiencies, secondary, in mucoviscidosis and celiac syndrome, *May*, 397
Deficits, fluid and electrolyte, unusual, table, *Nov.*, 877
Delivery, difficult, as cause of respiratory difficulty in newborn, *Nov.*, 854
type of, effect on premature mortality, *Aug.*, 574
Deodorants, poisoning by, *Nov.*, 782
Dermatitis, atopic, local treatment, *Nov.*, **963–968**
skin care, *Nov.*, 964
treatment of, ACTH and cortisone in, *Nov.*, **969–974**
principles, *Nov.*, 970
acute stage, *Nov.*, 965
medical, *Nov.*, 965
principles of, *Nov.*, 963
subacute phase, *Nov.*, 966
Development, degree of, effect on premature mortality, *Aug.*, 573
osseous, *May*, 472
Developmental study of prematurely born infants, *Aug.*, **679–684**
Diabetes mellitus as cause of growth failure, *May*, 441
Diabetic acidosis, fluid therapy in, *Nov.*, 884
treatment plan, table, *Nov.*, 885
Diagnosis, and management of coarctation of aorta, *Feb.*, **173–180**
clinical, of cyanotic congenital malformations of heart, *Feb.*, **131–146**
of congenital cardiovascular malformations unaccompanied by cyanosis, *Feb.*, **115–130**
Diaphragm, hernia of, *Nov.*, 909
Diarrhea, and septicemia in infant, *May*, 344
as symptom of milk allergy in infants, *Nov.*, 954
effect of water without sodium salts, *May*, 347
in infancy, fluid therapy in, *Nov.*, 880
treatment, *May*, **335–348**
antibacterial, *May*, 335
emergency, *May*, 340
maintenance, *May*, 341
principles of, *May*, 338
specific plan of, *May*, 340
treatment of physiologic disturbances, *May*, 336
treatment plan, table, *Nov.*, 881
with iron deficiency anemia, *May*, **345**
infectious, chronic, vs. allergic celiac syndrome, *Nov.*, 1014
Diet, in management of acute asthma, *Nov.*, 976
nursing mother's, relation to milk allergy in infant, *Nov.*, 958
supplemented, and delivery time of obese patients, *Aug.*, 700
and prematurity, table, *Aug.*, 696
and size of baby, *Aug.*, 703
birth weight in relation to, table, *Aug.*, 703
Digifolin in supraventricular paroxysmal tachycardia, *Feb.*, 225
Digitoxin, in paroxysmal tachycardia, *Nov.*, 864
in supraventricular paroxysmal tachycardia, *Feb.*, 225
Dipenicillin G in streptococcal infections, *May*, 411
Diphtheria, *Nov.*, 816
immunization, *May*, 351
booster or recall, *May*, 360
primary, *May*, 360
treatment with immune substances, *May*, 416
Discipline in accident prevention, *Nov.*, 762
Domination as cause of behavior problems, *May*, 461
Dosage in treatment of pollinosis, *Nov.*, **1039–1046**. See also *Pollinosis*.
Drainage, postural, *Aug.*, 631
Drowning, prevention, in toddlers, *Nov.*, 765
Drug therapy of acute asthma, *Nov.*, 976
Drugs used in pediatric cardiac emergencies, dosages, table, *Nov.*, 863

Ductus arteriosus, patent, and coarctation of aorta, pathology, *Feb.*, 17
angiocardiography in, *Feb.*, 86
aortography in, *Feb.*, 88
cardiac catheterization in, *Feb.*, 99
diagnosis, *Feb.*, 116, 159
murmurs, *Feb.*, 10
pathology, *Feb.*, 17
treatment, surgical, *Feb.*, **159–171**
with pulmonary hypertension, pathology, *Feb.*, 39
Dwarfism, pituitary, *May*, 441
Dyes, aniline, poisoning by, *Nov.*, 780

Ears, eyes and hands in diagnosis of heart disease, *Feb.*, **3–12**
Eating and cooking utensils for poliomyelitis patients, care of, *May*, 490
Ebstein's disease. See *Tricuspid valve*.
Eczema. See also *Dermatitis, atopic*.
acute, simple, treatment, *Nov.*, 965
as symptom of milk allergy in infants, *Nov.*, 952
atopic, *Nov.*, 927
chronic, treatment, *Nov.*, 967
exudative, acute, treatment, *Nov.*, 965
subacute, treatment, *Nov.*, 966
Edema, in erythroblastotic premature infant, *Aug.*, 547
infraorbital, in allergic tension-fatigue syndrome, *Nov.*, 1032
of brain, acute, treatment, *Nov.*, 794
pulmonary, in poliomyelitis, *May*, 492
mechanical aids for, *May*, 495
treatment, *May*, 493
Eisenmenger complex, angiocardiography in, *Feb.*, 87
diagnosis, *Feb.*, 142
pathology, *Feb.*, 36
surgical treatment, *Feb.*, 212
Electrocardiogram. See *Heart, electrocardiography*.
Electroencephalography in convulsions, *Nov.*, 805
Electrolyte and fluid management in children, *Nov.*, **873–899**. See also *Fluid and electrolyte management*.
Electrolyte disturbances, specific, *Nov.*, 888
Electrolyte imbalance in erythroblastotic premature infant, *Aug.*, 547
Electrosurgical resuscitation, *Nov.*, 852
Emergencies, and accidents, symposium on, *Nov.*, **757–918**
of respiratory tract in infants and children, *Nov.*, **811–826**
Emotional needs of children, *May*, 457
Emphysema, lobar, pulmonary resection for, *Aug.*, 713
Endocrine glands, diseases, as cause of retarded growth, *May*, 441
dysfunction vs. allergic tension-fatigue syndrome, *Nov.*, 1033
Endocrine glands, influences on growth and development, *May*, 468
Environment in management of acute asthma, *Nov.*, 975
Eosinophilia, stool, in allergic celiac syndrome, *Nov.*, 1010
Ephedrine, in asthma, *Nov.*, 818, 977
in Stokes-Adams syndrome, *Nov.*, 871
Epilepsy, allergic, *Nov.*, 1020
Epinephrine in asthma, *Nov.*, 817
Epinephrine hydrochloride in acute asthma, *Nov.*, 978, 979
Erythema annulare in rheumatic fever, *Feb.*, 6, 251
Erythroblastosis fetalis. See *Hemolytic disease of newborn*.
Erythrocyte(s), destruction, in premature infant, *Aug.*, 597
formation, in premature infant, *Aug.*, 596
normal values, in infants and children, *May*, 367
Erythrogenesis imperfecta. See *Anemia, hypoplastic, congenital*.
Erythromycin in diphtheria, *Nov.*, 817
Erythromycin stearate in acute asthma, *Nov.*, 981
Esophagus, atresia, in newborn, *May*, 304
complications, *May*, 307
treatment, *May*, 306
in premature infant, *Aug.*, 577
with or without tracheo-esophageal fistula, *Nov.*, 908
chalasia, in newborn, *May*, 307
stenosis, in newborn, *May*, 307
Ether in oil in status asthmaticus, *Nov.*, 819
Eve rocking device, *Nov.*, 825
Exposure as factor in poliomyelitis, *May*, 487
Extradural hemorrhage, treatment, *Nov.*, 793
Extrasystoles. See *Arrhythmias, cardiac*.
Eyes, hands and ears in diagnosis of heart disease, *Feb.*, **3–12**

Face, abrasions and lacerations, office treatment, *Nov.*, 788
Fallot, tetralogy of, angiocardiography in, *Feb.*, 78
cardiac catheterization in, *Feb.*, 103
diagnosis, *Feb.*, 138
pathology, *Feb.*, 34
surgical treatment, *Feb.*, 204
Falls, prevention, in toddlers, *Nov.*, 766
Family history in differential diagnosis of mucoviscidosis and celiac syndrome, *May*, 392
Fatalities, prevention in convulsions, *Nov.*, 806
Fatigue in allergic tension-fatigue syndrome, *Nov.*, 1031
Feces in celiac syndrome and mucoviscidosis, *May*, 396

Feeding of premature infant, *Aug.*, 582, 642
Ferrous sulfate poisoning, *Nov.*, 780
Fetus, death of, antepartum, effect on prematurity, *Aug.*, 520
Fever in diagnosis of rheumatic fever, *Feb.*, 253
Fibroelastosis, congenital, electrocardiographic patterns, *Feb.*, 63
endocardial, *Feb.*, 22, 243
laboratory findings, *Feb.*, 244
pathology, *Feb.*, 244
symptoms and signs, *Feb.*, 244
treatment, *Feb.*, 244
endomyocardial, *Feb.*, 22
Fidgets, tics and chorea, *Feb.*, 259
Fistula, arteriovenous, pulmonary, pathology, *Feb.*, 49
tracheo-esophageal, *Nov.*, 822
Fluid(s), administration, routes of, *Nov.*, 880
and electrolyte management, deficit requirements, time sequence for administration of, *Nov.*, 877
deficit therapy, *Nov.*, 877
in children, *Nov.*, **873–899**
maintenance therapy, *Nov.*, 873
replacement of contemporary losses, *Nov.*, 878
and electrolyte requirements, calculation from caloric estimate, *Nov.*, 875
and electrolyte solutions, comparison, table, *Nov.*, 896, 897
balance, influence of supersaturated atmosphere on, *Aug.*, 635
feeding of premature infant, *Aug.*, 643
in diabetic acidosis, *Nov.*, 884
therapy, in phase I of thermal burns, *Nov.*, 903
in preoperative and postoperative management, *Nov.*, 886
in specific diseases, *Nov.*, 880
Fluoride, sodium, poisoning by, *Nov.*, 774
Food, and air passages, foreign bodies in, *Nov.*, **827–843**. See also *Foreign bodies.*
reactions, allergenic, *Nov.*, 927
skin testing to, in allergy, *Nov.*, 935
trial ingestion, in gastrointestinal allergy, *Nov.*, 1003
Food, dairy, in gastrointestinal allergy, *Nov.*, 1002
Foramen ovale, premature closure, pathology, *Feb.*, 30
patent, with pulmonary valvular stenosis, angiocardiography in, *Feb.*, 80
Foreign bodies in air and food passages, *Nov.*, **827–843**
age distribution, table, *Nov.*, 829
anatomic location, table, *Nov.*, 829
classification, table, *Nov.*, 829
Foreign bodies in air and food passages, diagnosis, *Nov.*, 837
etiology, *Nov.*, 827
pathology, *Nov.*, 835
symptoms, *Nov.*, 831
treatment, *Nov.*, 838
Forethought in accident prevention, *Nov.*, 762
Friction rub. See under *Heart.*
Friedreich's ataxia, *Feb.*, 260

GAGGING as symptom of milk allergy in infants, *Nov.*, 955
Gamma globulin. See *Globulin.*
Gantrisin in meningitis, *May*, 413, 414
Garbage. See *Refuse.*
Gas pattern, normal, of intestines, *Nov.*, 911
Gasoline poisoning, *Nov.*, 774
Gastrointestinal aspiration of newborn, *Nov.*, 846
Gastrointestinal fluids, composition of, table, *Nov.*, 879
Gastrointestinal manifestations of allergy in children, *Nov.*, **995–1005**. See also *Allergy, gastrointestinal.*
Gastrointestinal tract, congenital anomalies, as cause of retarded growth, *May*, 440
effect on premature mortality, *Aug.*, 577
duplications, in newborn, *May*, 313
treatment, *May*, 314
Genitalia, external, development in adolescence, *May*, 475
Gentian violet in acute exudative eczema, *Nov.*, 965
Gestation, length of, *Aug.*, 698
prematurity by length of, *Aug.*, 692
Giardia infestation vs. allergic celiac syndrome, *Nov.*, 1014
Globulin, gamma, for poliomyelitis, *May*, 501
in infectious hepatitis immunization, reactions to, *May*, 358
Glucose, in diarrhea in infancy, *May*, 340
in status asthmaticus, *Nov.*, 983
Glycogen storage disease, *Feb.*, 239
diagnosis, *Feb.*, 124
electrocardiographic patterns, *Feb.*, 62
treatment, *Feb.*, 242
Gowns for care of poliomyelitis patients, *May*, 489
Gravity aspiration of newborn, *Nov.*, 847
Growth, and development, endocrine influences on, *May*, 468
failure, *May*, 433–446
diagnosis, *May*, 445
determining validity of, *May*, 433
in adolescence, *May*, 480
treatment, *May*, 445
physical, *May*, 469
rate of, relation to hematopoiesis, *Aug.*, 598

Growth, retarded, causes, *May*, 437
Growth record of premature infant, *Aug.*, **685–686**

Habit spasms, *Feb.*, 260
Hair, development in adolescence, *May*, 474
Hands, ears and eyes in diagnosis of heart disease, *Feb.*, **3–12**
Handwashing techniques for care of poliomyelitis patients, *May*, 490
Hay fever, *Nov.*, 927
Head injuries in children, *Nov.*, **787–799**
  hospital treatment, *Nov.*, 789
  office treatment, *Nov.*, 788
  office versus hospital treatment, *Nov.*, 787
Headaches, allergic, *Nov.*, 1018
Heart, anomalies, congenital, acyanotic
  diagnosis, *Feb.*, **115–130**
  as cause of retarded growth, *May*, 440
  cyanotic, diagnosis, *Feb.*, **131–146**
  cyanotic forms associated with right ventricular hypertrophy, pathology, *Feb.*, 33
  electrocardiogram in, *Feb.*, **51–71**
anomalies explored, *Feb.*, 148
block, *Feb.*, 231
  Adams-Stokes attack, *Feb.*, 233
  auriculoventricular, *Feb.*, 231
    congenital, *Feb.*, 232
  sino-auricular, *Feb.*, 231
catheterization, clinical, in infants and children, *Feb.*, **93–113**
disease, acyanotic, pathology, *Feb.*, 14
  clinical studies, value of, *Feb.*, 12
  congenital, electrocardiogram in differential diagnosis, *Feb.*, 64
  pathology, *Feb.*, **13–49**
  P wave contour in, *Feb.*, 64
  cyanotic, persistent, pathology, *Feb.*, 32
    with decreased pulmonary markings, electrocardiogram in differential diagnosis, *Feb.*, 66
  diagnosis, auscultation, *Feb.*, 8
  eyes, hands and ears in, *Feb.*, **3–12**
  history, *Feb.*, 3
  inspection, *Feb.*, 5
  palpation, *Feb.*, 6
  percussion, *Feb.*, 7
  physical examination, *Feb.*, 5
electrocardiography, in congenital malformations, *Feb.*, **51–71**
  in diagnosis of cyanotic congenital malformations, *Feb.*, 137
  in differential diagnosis of congenital heart disease, *Feb.*, 64
  normal, *Feb.*, 52
failure, congestive, acute, *Nov.*, 867
  management, *Nov.*, 868
fluoroscopic and roentgenographic examinations, *Feb.*, 135
Heart, friction rub, *Feb.*, 10
  glycogen storage disease. See under *Glycogen*.
  hypertrophy, *Feb.*, 134
  diagnosis, *Feb.*, 12
  electrocardiographic patterns, *Feb.*, 60
  idiopathic, electrocardiographic patterns, *Feb.*, 59
  in infancy, *Feb.*, **235–250**
  murmurs, *Feb.*, 8
  congenital, *Feb.*, 10
  functional, *Feb.*, 8, 254
  in diagnosis of rheumatic fever, *Feb.*, 254
  organic, *Feb.*, 8, 256
  significance, *Feb.*, 134
  position, anomalies of, electrocardiographic patterns, *Feb.*, 68
  rhabdomyoma, congenital. See under *Rhabdomyoma*.
  strain, combined, electrocardiographic patterns, *Feb.*, 63
  electrocardiographic patterns, adaptation type, *Feb.*, 52, 55
    barrage type, *Feb.*, 52, 55, 57
    surcharge type, *Feb.*, 52, 56
  left, electrocardiographic patterns, *Feb.*, 59
  right, electrocardiographic patterns, *Feb.*, 52
  surgery, anesthesia for, *Feb.*, **147–157**
  vascular markings, *Feb.*, 135
Heat, moist, for poliomyelitis patients, *May*, 490
Hematoma, of scalp, treatment, *Nov.*, 788
  subdural, treatment, *Nov.*, 795
Hemoglobin, degradation, in premature infant, *Aug.*, 597
  level of, prematurity and, *Aug.*, 707
  normal values, in infants and children, *May*, 367
  synthesis, in premature infant, *Aug.*, 596
Hemolytic disease of newborn, *May*, **283–302**, 388
  clinical manifestations, *May*, 285
  complications, *May*, 287
  conditions simulating, *May*, 288
  differential diagnosis, *May*, 287
  in premature infant, *Aug.*, **541–554**
    after-care, *Aug.*, 544
    antenatal measures, *Aug.*, 541
    treatment, *Aug.*, 542
  laboratory findings, *May*, 285
  pathogenesis, *May*, 284
  prognosis, *May*, 287
  treatment, *May*, 289
Hemorrhage, adrenal, in newborn, *May*, 331
  extradural, treatment, *Nov.*, 793
  in erythroblastotic premature infant, *Aug.*, 548

Hemorrhage, inapparent, from fetal surface of placental-uterine junction into maternal circulation, *Aug.*, 566
subarachnoid, treatment, *Nov.*, 796
subdural, treatment, *Nov.*, 795
Hepatitis, infectious, immunization, *May*, 356
reactions, *May*, 358
Heredity as cause of retarded growth, *May*, 437
Hernia, diaphragmatic, *Nov.*, 909
in newborn premature, *Aug.*, 579
inguinal, incarcerated, in newborn, *May*, 315
Herpes simplex, *Nov.*, 927
Hirschsprung's disease. See *Megacolon, congenital.*
History in gastrointestinal allergy, *Nov.*, 1000
Hives. See *Angioedema; Urticaria.*
Hormones, in infectious diseases, *May*, 419
salt and water, in newborn, *May*, 326
Hyaline membrane disease, prevention, *Aug.*, 538
Hyaline membrane, pulmonary, *Aug.*, 645
Hyaluronidase for parenteral fluid therapy in premature infant, *Aug.*, 655, 675
Hydration in status asthmaticus, *Nov.*, 983
Hydrocephalus in newborn premature, *Aug.*, 577
Hydrocortisone in asthma, table, *Nov.*, 820
Hydrolability in celiac syndrome and mucoviscidosis, *May*, 397
Hygiene, poor, as cause of retarded growth, *May*, 444
Hygroma, subdural, treatment, *Nov.*, 796
Hyperhidrosis in allergic tension-fatigue syndrome, *Nov.*, 1032
Hyperkalemia, *Nov.*, 889
Hypernatremia, *Nov.*, 891
causes, table, *Nov.*, 892
Hyperosmolarity, in infants, treatment, *May*, 343
with edema and hypocalcemia, *May*, 346
Hypertension, pulmonary, secondary to increased pulmonary flow, diagnosis, *Feb.*, 129
with patent ductus arteriosus, pathology, *Feb.*, 39
Hypertrophy. See *Heart; Ventricle.*
Hypokalemia, *Nov.*, 888
causes, table, *Nov.*, 889
Hyponatremia, *Nov.*, 890
Hypothermia as cause of respiratory difficulty in newborn, *Nov.*, 855
Hypothyroidism as cause of growth failure, *May*, 441

Ileus, meconium. See *Meconium ileus.*
Iliotycin suspension in acute asthma, *Nov.*, 981
Illegitimacy as cause of retarded growth, *May*, 438
Immaturity, degree of, effect on premature mortality, *Aug.*, 573
Immune substances in treatment of infectious diseases, *May*, 416
Immunization, *May*, **349–365**
general considerations, *May*, 358
procedures, combined, recommended, *May*, 359
program for infants, *May*, 360
reactions, *May*, 357
Independence, emotional need of children for, *May*, 459
Individual, acceptance as, emotional need of children for, *May*, 458
Infancy, accident prevention in, *Nov.*, 763
anemias of, *May*, **367–388**. See also *Anemias.*
diarrhea in, treatment, *May*, **335–348**. See also *Diarrhea.*
megaloblastic anemia of, *May*, 379
Infants, immunization program, table, *May*, 360
newborn. See *Newborn.*
premature. See *Premature infant; Prematurity.*
Infection, as cause of retarded growth, *May*, 443
prevention in premature infants, *Aug.*, 538, 584, 644
vs. allergic tension-fatigue syndrome, *Nov.*, 1033
Infectious diseases, causative agents, table, *May*, 409
efficacy of therapeutic agents, table, *May*, 406
treatment, specific, *May*, **405–420**
Infraorbital edema in allergic tension-fatigue syndrome, *Nov.*, 1032
Infundibular stenosis, punch valvulotomy for, *Feb.*, 208
Inhalants, skin tests to, *Nov.*, 937
Injuries, head, in children, *Nov.*, **787–799**
prevention in convulsions, *Nov.*, 806
Insecticides, poisoning by, *Nov.*, 781
Insulin in diabetic acidosis, *Nov.*, 884
Intermittent negative pressure, *Nov.*, 851
Intermittent positive pressure, *Nov.*, 850
Intestine(s), atresia of, *Nov.*, 913
in newborn, *May*, 312
in premature infant, *Aug.*, 578
normal gas pattern, *Nov.*, 911
obstruction of, in early infancy, *Nov.*, **907–918**
in newborn infant, *May*, **303–320**
small, roentgen studies of, in allergic celiac syndrome, *Nov.*, 1011
stenosis, in newborn, *May*, 312
in premature infant, *Aug.*, 578
Intoxication, barbiturate, *Nov.*, 775
potassium, *Nov.*, 889
salicylate, *Nov.*, 776

Intussusception in newborn, *May*, 315
treatment, *May*, 316
Ipecac, syrup of, in acute asthma, *Nov.*, 978
Iron deficiency anemia. See *Anemia*.
Iron therapy, for premature infant, *Aug.*, 583, 672
in anemia of prematurity, *Aug.*, 599
Isonicotinic acid hydrazide in tuberculous meningitis, *May*, 415
Isuprel in asthma, *Nov.*, 818, 979

JAUNDICE in erythroblastotic premature infant, *Aug.*, 549
Joint pains in diagnosis of heart disease, *Feb.*, 5

KERNICTERUS, *May*, 288
in erythroblastotic premature infant, *Aug.*, 550
Kerosene poisoning, *Nov.*, 774
17-Ketosteroids, physiology, in newborn, *May*, 325
Kidneys, congenital anomalies as cause of retarded growth, *May*, 440

LABOR, premature, anemia and, *Aug.*, 706
premature induction, in erythroblastosis fetalis, *Aug.*, 551
contraindications, *Aug.*, 552
indications, *Aug.*, 552
management of, *Nov.*, 856
Laboratory tests, routine, in premature infants, *Aug.*, 642
Lanatoside C in paroxysmal tachycardia, *Nov.*, 864
Laryngotracheobronchitis, acute, *Nov.*, 813
Larynx, obstruction of, *Nov.*, 812
Lead poisoning, *Nov.*, 776
Leukocytosis in diagnosis of rheumatic fever, *Feb.*, 260
Linen, care of, for poliomyelitis patients, *May*, 490
Liver, congenital anomalies as cause of retarded growth, *May*, 440
Love, lack of, as cause of behavior problems, *May*, 459
Lungs, congenital anomalies as cause of retarded growth, *May*, 440
cysts, congenital, pulmonary resection for, *Aug.*, 714
fetal, importance of degree of maturation, *Aug.*, 529
oxygenation in resuscitation of newborn premature, *Aug.*, 535
Lutembacher syndrome, *Feb.*, 27, 28
Lye poisoning, *Nov.*, 773

MAGNESIUM sulfate in acute congestive failure, *Nov.*, 868
Malformations. See *Abnormalities*.
Malignancy as cause of retarded growth, *May*, 444
Malnutrition, emotional, as cause of retarded growth, *May*, 443
maternal, as cause of retarded growth, *May*, 438
physical, as cause of retarded growth, *May*, 442
vs. allergic tension-fatigue syndrome, *Nov.*, 1033
Malrotation with midgut volvulus, *Nov.*, 916
Maternal factors in prematurity, *Aug.*, **515–526**
Meconium ileus, *Nov.*, 916
in mucoviscidosis, *May*, 398
in newborn, *May*, 314
Medical care, effect on premature mortality, *Aug.*, 580
Mediterranean anemia. See *Thalassemia*.
Megacolon, *Nov.*, 917
congenital, in newborn, *May*, 316
treatment, *May*, 317
Membranes, rupture of, premature, treatment, *Nov.*, 856
Meningeal allergy, *Nov.*, 1023
Meningitis, bacterial, etiology, undetermined, treatment, *May*, 413
E. coli, treatment, *May*, 413
H. influenzae, treatment, *May*, 413
meningococcal, treatment, *May*, 414
pneumococcal, treatment, *May*, 414
purulent, treatment, *May*, 411
tuberculous, treatment, *May*, 414
Menstruation and menstrual disorders in adolescence, *May*, 476
Metabolic acidosis, *Nov.*, 894
Metabolic alkalosis, *Nov.*, 895
Metabolic rate, basal, table, *Nov.*, 874
Metabolism, errors of, inborn, as cause of retarded growth, *May*, 442
Midgut, malrotation, in newborn, *May*, 310
treatment, *May*, 311
Milk allergy, cow's, in infants, *Nov.*, **949–962**
diagnostic trial test, *Nov.*, 959
differential diagnosis, *Nov.*, 959
family history, *Nov.*, 959
symptoms, *Nov.*, 952
development of, table, *Nov.*, 952
table, *Nov.*, 953
Milk mixtures, composition of, table, *Aug.*, 654
Mist therapy. See *Nebulization therapy*.
Mitral valve, accessory tissue, pathology, *Feb.*, 25
atresia, pathology, *Feb.*, 40
diastolic rumble, *Feb.*, 9
insufficiency, pathology, *Feb.*, 24
murmurs, *Feb.*, 8
presystolic, *Feb.*, 9
systolic, *Feb.*, 9
stenosis, and atrial septal defect, pathology, *Feb.*, 27
pathology, *Feb.*, 25

Morphine sulfate, in anoxic spells, *Nov.*, 866
in paroxysmal tachycardia, *Nov.*, 864
preoperative, in cardiac surgery, *Feb.*, 151
Mortality, premature infant, factors influencing, *Aug.*, **573–583**
Moth repellents, poisoning by, *Nov.*, 779
Mucoviscidosis, and celiac syndrome, *May*, **389–403**
bacteriologic studies, *May*, 400
clinical variants, *May*, 402
diagnosis, *May*, 392
differential diagnosis, *May*, 392
laboratory investigation, *May*, 398
onset, age at, *May*, 395
prognosis, *May*, 402
symptoms and signs, *May*, 395
treatment, *May*, 401
with partial pancreatic insufficiency, *May*, 399
Mucus, in throat, excess, as symptom of milk allergy in infants, *Nov.*, 955
Mumps, immunization, *May*, 357
Murmurs, cardiac. See under *Heart*.
Mushroom poisoning, *Nov.*, 781
Myocarditis, *Feb.*, 245
isolated, diagnosis, *Feb.*, 124
pathology, *Feb.*, 246
symptoms, signs and laboratory findings, *Feb.*, 246
treatment, *Feb.*, 247

Naphtha poisoning, *Nov.*, 774
Nasal allergy, *Nov.*, 988
Nasopharyngeal aspiration of newborn, *Nov.*, 846
Nebulization therapy, continuous, *Aug.*, **625–638**
apparatus, *Aug.*, 628
indications for, *Aug.*, 635
techniques, *Aug.*, 628
theory for, *Aug.*, 627
results, *Aug.*, 641
Nembutal in acute asthma, *Nov.*, 979
Neomycin in acute exudative eczema, *Nov.*, 965
Neonatal deaths, number and percentage distribution, table, *Aug.*, 528
Nerves, cranial, in poliomyelitis, *May*, 486
Nervous system, central, congenital anomalies as cause of retarded growth, *May*, 439
congenital malformations, effect on premature mortality, *Aug.*, 577
disorders of vs. allergic tension-fatigue syndrome, *Nov.*, 1033
Neuritic allergy, *Nov.*, 1023
Neurologic allergy in childhood, *Nov.*, **1017–1027**. See also *Allergy, neurologic*
Newborn, adrenal physiology, *May*, **321–334**
Newborn, handicapped, resuscitation of, *Nov.*, 856
hemolytic disease of. See *Hemolytic disease*.
obstructive lesions of intestinal tract in, *May*, **303–320**
respiratory difficulty in, causes, *Nov.*, 853
respiratory problems in, management, *Nov.*, 856
resuscitation of, *Nov.*, **845–858**. See also *Resuscitation of newborn*.
Niacinamide for premature infant, *Aug.*, 655, 671
Nicotine poisoning, *Nov.*, 781
Nodules, rheumatic, in rheumatic fever, *Feb.*, 252
Noroisodrine in asthma, *Nov.*, 818
Nose, obstruction of, *Nov.*, 812
Nose colds as symptom of milk allergy, *Nov.*, 956
Nose drops in acute asthma, *Nov.*, 976
Nursery technique for premature infant, *Aug.*, 641
Nursing care, effect on premature mortality, *Aug.*, 580
Nutrient supplements during pregnancy, effect on incidence of prematurity, *Aug.*, 695
Nutrition, and nutritional deficiencies related to premature infant, *Aug.*, **687–708**
disturbances of, in mucoviscidosis and celiac syndrome, *May*, 396
gastrointestinal allergy and, *Nov.*, 999
problems, in adolescence, *May*, 478

Obesity in adolescence, *May*, 479
Operation, Your Child's, *Aug.*, **721–742**
Ostium, infundibular, stenosis of, pathology, *Feb.*, 31
Otitis media, treatment, *May*, 409
Ovarian agenesis as cause of growth failure, *May*, 441
Overprotection as cause of behavior problems, *May*, 460
Oxygen, for premature infant, *Aug.*, 640
gastrointestinal, in resuscitation, *Nov.*, 852
in asthma, *Nov.*, 818, 819
in status asthmaticus, *Nov.*, 983
reduction, and development of hypoxic retinopathy, *Aug.*, 617
requirements, of premature infant, maintenance, *Aug.*, 614
of retina. See *Retina*.
studies, blood, in premature, *Aug.*, **587–591**
toxicity, as cause of respiratory difficulty in newborn, *Nov.*, 855
weaning of infants from, *Aug.*, 621
Oxygen therapy for premature infant, *Aug.*, 583
Oxygenation of lungs in resuscitation of newborn premature, *Aug.*, 535

P.A.S. See *Acid, para-aminosalicylic.*
P wave contour in congenital heart disease, *Feb.*, 63
Pacemaker, wandering, *Feb.*, 215, 218
Pain, abdominal, as symptom of gastrointestinal allergy, *Nov.*, 998
joint, in diagnosis of heart disease, *Feb.*, 5
leg, in diagnosis of rheumatic fever, *Feb.*, 253
Pallor in allergic tension-fatigue syndrome, *Nov.*, 1032
Pancreas, annular, *Nov.*, 916
cystic fibrosis, vs. allergic celiac syndrome, *Nov.*, 1013
Paraldehyde in convulsive seizures, *Nov.*, 809
Parents, attitudes toward children, *May*, 459
Patch test for allergy, *Nov.*, 939
Pathology, functional, of congenital cardiac disease, *Feb.*, **13–49**
Penicillin, aerosol solutions, *Aug.*, 634
in laryngotracheobronchitis, *Nov.*, 814, 815
in meningitis, *May*, 413, 414
in rheumatic fever, recurrent, prophylaxis, *Feb.*, 273
in streptococcal infections, *May*, 411
prophylactic, for premature infant, *Aug.*, 538, 584, 644, 656
sensitivity to skin testing for, *Nov.*, 940
significance, *Nov.*, 941
Penicillin G, procaine, in acute asthma, *Nov.*, 981
Pericardial cavity, exploration, *Feb.*, 199
Pericardial tamponade, *Nov.*, 869
Pericardium, defects of, pathology, *Feb.*, 30
Peritoneal bands in newborn, *May*, 310
treatment, *May*, 311
Pertussis, immunization, *May*, 353, 361
passive, *May*, 361
reactions, *May*, 358
results, table, *May*, 355
treatment with immune substances, *May*, 417
Pharynx, obstruction of, *Nov.*, 812
Phosphate, organic, poisoning by, *Nov.*, 781
Phosphorus poisoning, *Nov.*, 782
Placenta, blood vessels of, incision into, at cesarean section, *Aug.*, 559
Placenta previa, *Aug.*, 555
Plasma. See *Blood plasma.*
Pleural cavity, exploration, *Feb.*, 199
Pneumonia, *Nov.*, 819
Pneumothorax, *Nov.*, 823
Poisoning, accidental, *May*, 426
in infants and children, *Nov.*, **771–786**
prevention, *Nov.*, 784
treatment, general principles, *Nov.*, 783
prevention, in toddlers, *Nov.*, 767
Poliomyelitis, 1954, *May*, **483–501**
abortive, symptoms, *May*, 484
after-care, *May*, 499
objective, *May*, 500
bulbar, *May*, 485
danger signals in respirator, *May*, 496
treatment, *May*, 491
bulbospinal, *May*, 486
case reporting, *May*, 488
cerebrospinal fluid findings, *May*, 487
clinical manifestations, *May*, 486
communicability, *May*, 484
control, *May*, 488
criteria for discharge of patient, *May*, 499
definition, *May*, 483
diagnosis, *May*, 484
epidemiology, *May*, 484
equipment, essential, *May*, 489
follow-up services, *May*, 499
history in case finding, *May*, 487
home care, *May*, 488
hospitalization, *May*, 488
period of, *May*, 499
immunity, *May*, 484
incubation period, *May*, 483
isolation of patients, *May*, 488
isolation units, *May*, 489
mechanical aids in, *May*, 494
nonparalytic, symptoms, *May*, 485
occupational therapy, *May*, 499
paralytic, classifications, *May*, 485
symptoms, *May*, 485
patient care service, planning for, *May*, 499
patient care techniques, *May*, 489
physical therapy, *May*, 498
position of patient, *May*, 490
prevention, *May*, 500
quarantine, *May*, 488
respiratory problems associated with, *Nov.*, 822
sources of infection, *May*, 483
spinal, *May*, 485
susceptibility, *May*, 484
transmission, *May*, 484
treatment, *May*, 488
Pollen, dosage for children, table, *Nov.*, 1044
skin tests to, *Nov.*, 937
Pollinosis, treatment, dosage in, *Nov.*, **1039–1046**
maximum tolerated dosage, *Nov.*, 1039
recommended dosage, *Nov.*, 1042
results, *Nov.*, 1044
small dosage, *Nov.*, 1041
Polyethylene tube, indwelling, in feeding of premature infants, *Aug.*, 642
Posthemorrhagic shock in newborn premature, *Aug.*, **555–572**
Potassium, depletion, *Nov.*, 888
causes, table, *Nov.*, 889
intoxication, *Nov.*, 889
preparations, table, *Nov.*, 898

Potassium iodine in asthma, *Nov.*, 819
Potassium permanganate in acute exudative eczema, *Nov.*, 965
Potbelly in celiac syndrome and mucoviscidosis, *May*, 396
Precordial distress, *Feb.*, 258
Pregnancy, artificial termination, effect on prematurity, *Aug.*, 518
nutrient supplements during, effect on incidence of prematurity, *Aug.*, 695
premature termination, complications, table, *Aug.*, 519
weight gain in, *Aug.*, 689
first and second trimesters, *Aug.*, 690
Premature infant, anemia in, *Aug.*, **593–606**. See also *Anemia*.
anesthesia or analgesia in relation to blood oxygen saturation, *Aug.*, 589
apneic or asphyxiated, resuscitation, *Aug.*, 533
blood oxygen studies in, *Aug.*, **587–591**
blood transfusions in, *Aug.*, 583
care of, *Aug.*, **649–659**
alimentary phase, *Aug.*, 653
educational program, *Aug.*, 657
emergency phase, *Aug.*, 650
follow-up care, *Aug.*, 657
growth phase, *Aug.*, 655
newer concepts, *Aug.*, **639–648**
revised rules, *Aug.*, 658
specific measures, *Aug.*, 665
symposium on, *Aug.*, **513–708**
development study, *Aug.*, **679–684**
marital status, table, *Aug.*, 682
erythroblastosis fetalis in, *Aug.*, **541–554**. See also *Hemolytic disease of newborn*.
mental development, *Aug.*, 646
present status, table, *Aug.*, 680
erythroblastotic, disturbances of, management, *Aug.*, 544
estimated developmental ratings, table, *Aug.*, 684
fatality rate, table, *Aug.*, 680
feeding of, *Aug.*, 582, 642, 653, 669
standard formulas, table, *Aug.*, 671
growth record, *Aug.*, **685–686**
intrapartum deaths, *Aug.*, 523
maintenance of body heat, *Aug.*, 665
morbidity, acquired, treatment of, table, *Aug.*, 673
control and treatment, *Aug.*, 672
incidence, table, *Aug.*, 672
mortality, by weight, table, *Aug.*, 523
causes, *Aug.*, 524
factors influencing, *Aug.*, **573–586**
neonatal, *Aug.*, 522
and live births, table, *Aug.*, 517
mortality rates by ages, table, *Aug.*, 677
nutrition and nutritional deficiencies related to, *Aug.*, **687–708**
Premature infant, oxygen requirements, maintenance of, *Aug.*, 614
oxygen therapy, *Aug.*, 583, 666
pathology among, table, *Aug.*, 683
posthemorrhagic shock in, *Aug.*, **555–572**
prevention of hyaline membrane disease, *Aug.*, 538
prevention of infection, *Aug.*, 538, 584
respiration in, abnormal, technique for treatment, *Aug.*, **625–638**
establishment of, *Aug.*, 580, 666
resuscitation, *Aug.*, **527–539**
temperature adjustment, *Aug.*, 581
treatment at birth, *Aug.*, 640
Premature unit, autonomous, *Aug.*, **661–678**
economics, *Aug.*, 662
equipment, *Aug.*, 663
general policies, *Aug.*, 664
nursing personnel, *Aug.*, 664
plan of unit, *Aug.*, 663
results, *Aug.*, 676
Prematurity, *Aug.*, 702
and hemoglobin level, table, *Aug.*, 707
and supplemented diet, table, *Aug.*, 696
as cause of retarded growth, *May*, 438
by length of gestation, *Aug.*, 692
control of, *Nov.*, 856
definition, *Aug.*, 515
factors influencing, *Aug.*, 517
incidence, *Aug.*, 515
by birth weight groups, table, *Aug.*, 665
effect of nutrient supplements during pregnancy on, *Aug.*, 695
table, *Aug.*, 680
maternal factors in, *Aug.*, **515–526**
prevention, *Nov.*, 856
primary, *Aug.*, 520
Premedication for cardiac surgery, *Feb.*, 149
Prenatal care, rationale, *Aug.*, 639
Prenatal gain in weight and size of baby, *Aug.*, 693
Promizole in tuberculous meningitis, *May*, 415
Pronestyl in ventricular tachycardia, *Nov.*, 864
Propadrine hydrochloride in acute asthma, *Nov.*, 978
Prostigmin in paroxysmal tachycardia, *Feb.*, 227
Protein skin tests in allergy, *Nov.*, 946
Pseudotruncus communis, diagnosis, *Feb.*, 140
Psychic disturbances in mucoviscidosis and celiac syndrome, *May*, 397
Psychosomatics, essentials of, in allergic children, *Nov.*, **921–928**
Pulmonary hyaline membrane in premature infant, *Aug.*, 581, 645
Pulmonary resection in infants and children, *Aug.*, **709–720**
complications, *Aug.*, 719
incidence, table, *Aug.*, 710

Pulmonary valve, atresia, with intact ventricular septum, pathology, *Feb.*, 42
stenosis, cardiac catheterization in, *Feb.*, 104
diagnosis, *Feb.*, 128
isolated, pathology, *Feb.*, 30
murmurs, *Feb.*, 11
pure, angiocardiography in, *Feb.*, 87
syndromes resulting from, *Feb.*, 105
with cyanosis, surgical treatment, *Feb.*, 200
with intact ventricular septum and atrial septal defect, pathology, *Feb.*, 33
with interauricular communication, diagnosis, *Feb.*, 139
with patent foramen ovale, angiocardiography in, *Feb.*, 80
with poststenotic dilatation of pulmonary artery, interatrial septal defect and infundibular valvelike stenosis, surgical treatment, *Feb.*, 204
with reopening of foramen ovale or atrial septal defects, surgical treatment, *Feb.*, 200
Punch, valvulotomy for infundibular stenosis, *Feb.*, 208
Pylorospasm, as symptom of gastrointestinal allergy, *Nov.*, 999
as symptom of milk allergy in infants, *Nov.*, 953
Pylorus, stenosis of, fluid therapy in, *Nov.*, 882
in newborn, *May*, 308
diagnosis, *May*, 310
etiology, *May*, 309
treatment, *May*, 310
treatment plan, table, *Nov.*, 883
Pyribenzamine in acute asthma, *Nov.*, 980

Quinidine, in supraventricular paroxysmal tachycardia, prophylactic, *Feb.*, 227
in ventricular tachycardia, *Nov.*, 864
Quinidine sulfate in ventricular paroxysmal tachycardia, *Feb.*, 227, 228

Race as cause of retarded growth, *May*, 438
Rashes as symptom of milk allergy in infants, *Nov.*, 952
Recognition, emotional need of children for, *May*, 458
Rectum, atresia in newborn premature, *Aug.*, 578
prolapse, in mucoviscidosis, *May*, 396
stenosis of, in newborn premature, *Aug.*, 578
Refuse, disposal, in poliomyelitis, *May*, 490
Rejection as cause of behavior problems, *May*, 460
Respiration, abnormal, in premature infant, technique for treatment, *Aug.*, **625–638**
artificial, *Nov.*, 824
difficulty in, in erythroblastotic premature infant, *Aug.*, 545
establishment, in premature infant, *Aug.*, 580
physiology of, *Aug.*, 529
in poliomyelitis, *May*, 486
labored, in diagnosis of heart disease, *Feb.*, 4
muscles of, paralysis of, in poliomyelitis, *May*, 491
danger signals in respirator, *May*, 496
mechanical aids for, *May*, 494
treatment, *May*, 492, 493
of newborn premature infant, *Aug.*, **527–539**
Respirator, cuirass, *May*, 498
mechanical failure, *May*, 495
rates and pressure, *May*, 496
tank, mechanics of, *May*, 495
weaning of patient from, *May*, 497
precautions, *May*, 498
Respiratory acidosis, *Nov.*, 894
Respiratory alkalosis, *Nov.*, 894
Respiratory allergy. See *Allergy*.
Respiratory conditions, allergic, vaccine treatment in, value of, *Nov.*, **987–993**
Respiratory problems in newborn, management, *Nov.*, 856
Respiratory tract, diseases, acute, treatment, *May*, 405
disturbances, in mucoviscidosis, *May*, 395
emergencies, in infants and children, *Nov.*, **811–826**
lesions, obstructive, *Nov.*, 811
obstructed in poliomyelitis, *May*, 492
effect on respirator action, *May*, 495
mechanical aids for, *May*, 494
treatment, *May*, 493
obstructive diseases, signs and symptoms, table, *Nov.*, 812
open, provision of, in resuscitation of newborn premature, *Aug.*, 534
Resuscitation, manual, *Nov.*, 849
mechanical, *Nov.*, 850
of asphyxiated or apneic premature infant, *Aug.*, 533
of handicapped newborn, *Nov.*, 856
of newborn, *Nov.*, **845–858**
methods, *Nov.*, 849
Retina, oxygen requirements, *Aug.*, 610
in hypoxic infants, *Aug.*, 611
with oxygen administration, *Aug.*, 612
in normal infants, *Aug.*, 610
Retinopathy, hypoxic, and its sequel, *Aug.*, 607

Retinopathy, development of, oxygen reduction hypoxic, and, *Aug.*, 617
Retrolental fibroplasia, *Aug.*, **607–623**, 645
etiology, *Aug.*, 608
prevention, *Aug.*, 618
general measures, *Aug.*, 621
Rh factor, type, in hemolytic disease of newborn, *May*, 289, 290
Rhabdomyoma, congenital, *Feb.*, 242
electrocardiographic patterns, *Feb.*, 63
Rheumatic fever, acute, treatment, *Feb.*, 268
diagnosis, *Feb.*, **251–263**
recurrent, prevention of, *Feb.*, 273
treatment and prevention, *Feb.*, **265–274**
Riboflavin for premature infant, *Aug.*, 655, 671
Rocking bed, principle of, *May*, 498
Rocking device, Eve, *Nov.*, 825
Roentgenograms of chest in newborn, *Nov.*, 855
Roentgenography, cranial, in convulsions, *Nov.*, 806

Salicylate intoxication, *Nov.*, 776
Salt and water hormone in newborn, *May*, 326
Scalp, abrasions, treatment, *Nov.*, 788
hematomas, treatment, *Nov.*, 788
Sclerosis, endocardial, diagnosis, *Feb.*, 122
pathology, *Feb.*, 22
Scopolamine hydrobromide, preoperative use in cardiac surgery, *Feb.*, 151
Seconal, in acute asthma, *Nov.*, 979
in convulsive seizures, *Nov.*, 808
Section, cesarean, incision into placental or umbilical blood vessels at, *Aug.*, 559
Security, emotional need of children for, *May*, 458
Sedation, in acute asthma, *Nov.*, 979
in status asthmaticus, *Nov.*, 984
Self-respect, emotional need of children for, *May*, 458
Sepsis neonatorum, in premature infant, *Aug.*, 600
Septal defects, electrocardiogram in differential diagnosis, *Feb.*, 65
Septicemia and diarrhea in an infant, *May*, 344
Sex as cause of retarded growth, *May*, 437
Sex characters, secondary, development, *May*, 474
Sex organs, development, *May*, 474
Shock, minimization, in resuscitation of newborn premature, *Aug.*, 534
posthemorrhagic, in newborn premature, *Aug.*, **555–572**
traumatic, treatment, *Nov.*, 789
Shunt operations, for cardiovascular anomalies, *Feb.*, 208
for tetralogy of Fallot, *Feb.*, 204
Sickle cell disease, *May*, 386
Sickle cell trait, *May*, 386
Sinus, coronary, communication with left atrium, pathology, *Feb.*, 29
Sinus arrhythmia, *Feb.*, 215, 218
Sinus bradycardia, *Feb.*, 215, 218
Sinus tachycardia, *Feb.*, 215, 218, 257
Skeletal size in relation to dietary supplement, *Aug.*, 704
Skin, care of, in atopic dermatitis, *Nov.*, 964
Skin tests, and their value in pediatric allergy, *Nov.*, **929–942**
for allergy, changeableness, *Nov.*, 938
delayed reactions, *Nov.*, 939
diagnostic value, *Nov.*, 930
in atopic dermatitis, table, *Nov.*, 935
in first year of life, *Nov.*, 934
patch test, *Nov.*, 939
scout testing, *Nov.*, 933
skin testing to foods, *Nov.*, 935
substances to test for, *Nov.*, 933
technique, *Nov.*, 932
tests to inhalants and pollen, *Nov.*, 937
transfer testing, indirect or passive, *Nov.*, 934
for gastrointestinal allergy, *Nov.*, 1000
table, *Nov.*, 1001
for penicillin sensitivity, *Nov.*, 940
significance, *Nov.*, 941
in allergic celiac syndrome, *Nov.*, 1012
protein, for allergy, *Nov.*, 946
Skull, fracture, linear, treatment, *Nov.*, 788
treatment, *Nov.*, 796
Smallpox, immunization, *May*, 350
material and technique, *May*, 361
reactions, *May*, 358
Sodium amytal in convulsive seizures, *Nov.*, 809
Sodium fluoride poisoning, *Nov.*, 774
Sodium phenobarbital in convulsive seizures, *Nov.*, 807, 808, 809
Sodium sulfadiazine. See *Sulfadiazine*.
1, 2, 3-Solution in diarrhea in infancy, *May*, 340
Solutions for parenteral administration, *May*, 339
Spasms, habit, *Feb.*, 260
Spells in diagnosis of heart disease, *Feb.*, 4
Spherocytosis, hereditary, *May*, 383
Spina bifida, in newborn premature, *Aug.*, 577
Starch intolerance vs. allergic celiac syndrome, *Nov.*, 1013
Status asthmaticus, *Nov.*, 983
Steatorrhea, in allergic celiac syndrome, *Nov.*, 1010
infantile, idiopathic, vs. allergic celiac syndrome, *Nov.*, 1013

Stokes-Adams syndrome, *Nov.*, 870
Stool eosinophilia in allergic celiac syndrome, *Nov.*, 1010
Stramonium poisoning, *Nov.*, 777
Streptococcal infections, treatment, *May*, 410
Streptomycin, aerosol solutions, *Aug.*, 634
in laryngotracheobronchitis, *Nov.*, 814, 815
in tuberculous meningitis, *May*, 415
prophylactic, for premature infant, *Aug.*, 584, 656
Strychnine poisoning, *Nov.*, 782
Subaortic valve, stenosis, diagnosis, *Feb.*, 122
pathology, *Feb.*, 19
Subarachnoid hemorrhage, treatment, *Nov.*, 796
Subdural hematoma, treatment, *Nov.*, 795
Subdural hemorrhage, treatment, *Nov.*, 795
Subdural hygroma, treatment, *Nov.*, 796
Subdural puncture in convulsions, *Nov.*, 805
Sulfadiazine, in meningitis, *May*, 413, 414
in rheumatic fever, recurrent, prophylaxis, *Feb.*, 273
sodium, prophylactic, for premature infant, *Aug.*, 584, 644
Surgery, cardiac, anesthesia for, *Feb.*, **147–157**
postoperative care and complications, *Feb.*, 155
preoperative preparation, *Feb.*, 149
Sus-Phrine in acute asthma, *Nov.*, 979
Sydenham's chorea, *Feb.*, 259
Symptomless interval of foreign body in air and food passages, *Nov.*, 832
Syndrome, Lutembacher, *Feb.*, 27, 28
Systoles, premature, *Feb.*, 219

Tachycardia, paroxysmal, *Feb.*, 222, 258; *Nov.*, 859
diagnosis, *Nov.*, 862
electrocardiogram in, *Nov.*, 860
in young infants, Feb., 228
laboratory findings, *Nov.*, 860
management, *Nov.*, 862
prognosis, *Nov.*, 865
radiologic picture, *Nov.*, 860
repetitive, *Feb.*, 229
treatment, *Feb.*, 225
effect of, table, *Nov.*, 862
sinus, *Feb.*, 215, 218, 257
Tamponade, pericardial, *Nov.*, 869
Tar dermament in chronic eczema, *Nov.*, 967
Taussig-Bing syndrome, angiocardiography in, *Feb.*, 82
diagnosis, *Feb.*, 143
pathology, *Feb.*, 39
surgical treatment, *Feb.*, 212
Temperature adjustment in premature infant, *Aug.*, 581, 641
Tension in allergic tension-fatigue syndrome, *Nov.*, 1030
Tension-fatigue syndrome, allergic, *Nov.*, **1029–1037**. See also *Allergic tension-fatigue syndrome*.
Terramycin, in acute asthma, *Nov.*, 981
in acute exudative eczema, *Nov.*, 965
in laryngotracheobronchitis, *Nov.*, 815
Tetanus, immunization, active, *May*, 352
booster or recall, *May*, 361
passive, *May*, 361
primary, *May*, 360
reactions, *May*, 357
treatment with immune substances, *May*, 417
Tetracycline hydrochloride in laryngotracheobronchitis, *Nov.*, 815
Tetralogy of Fallot. See under *Fallot*.
Thalassemia, *May*, 385
Thiamine for premature infant, *Aug.*, 655, 671
Thorax, drainage, *Feb.*, 199
Thrill in diagnosis of heart disease, *Feb.*, 7
Throat, sore, in diagnosis of heart disease, *Feb.*, 5
Tics, *Feb.*, 260
chorea and fidgets, *Feb.*, 259
Time in accident prevention, *Nov.*, 762
Toadstool, poisoning by, *Nov.*, 781
Tocopherol for premature infant, *Aug.*, 655
Toddlers, accident prevention in, *Nov.*, 764
Toxemia, as symptom of milk allergy in infants, *Nov.*, 957
effect on prematurity, *Aug.*, 520
Trachea, obstruction of, *Nov.*, 812
Tracheobronchial aspiration of newborn, *Nov.*, 846
Tracheo-esophageal fistula, *Nov.*, 822
in newborn premature, *Aug.*, 577
without atresia, *May*, 307
Trauma, multiple, as cause of retarded growth, *May*, 444
Traumatic factors in poliomyelitis, *May*, 487
Tribromoethanol in convulsive seizures, *Nov.*, 809
Tricuspid valve, atresia, angiocardiography in, *Feb.*, 83, 85
diagnosis, *Feb.*, 139
in newborn premature, *Aug.*, 580
pathology, *Feb.*, 46
surgical treatment, *Feb.*, 207
with complete transposition of great vessels, diagnosis, *Feb.*, 143
murmurs, *Feb.*, 9
stenosis, diagnosis, *Feb.*, 139
in newborn premature, *Aug.* 580
with complete transposition of great vessels, diagnosis, *Feb.*, 143
with interauricular communication (cyanotic type), diagnosis, *Feb.*, 140

Truncus arteriosus communis, diagnosis, *Feb.*, 142
persistent, angiocardiography in, *Feb.*, 85
pathology, *Feb.*, 37
surgical treatment, *Feb.*, 212
Tuberculosis, immunization, *May*, 356
reactions to BCG, *May*, 358
Twins, effect on prematurity, *Aug.*, 518
Typhoid fever, immunization, *May*, 355, 362
reactions, *May*, 358

Umbilical cord care, *Nov.*, 848
Umbilicus, blood vessels of, incision into, at cesarean section, *Aug.*, 559
ruptures in, *Aug.*, 561
treatment, *Aug.*, 566
Underweight in adolescence, *May*, 480
Urine, examinations, in convulsions, *Nov.*, 805
volume, hourly, in thermal burns, *Nov.*, 904
Urticaria, *Nov.*, 927
as symptom of milk allergy in infant, *Nov.*, 957

Vaccination, smallpox. See *Smallpox, immunization.*
Vaccine, alum-precipitated or aluminum hydroxide absorbed, *May*, 357
autogenous, in respiratory allergy, dosage, *Nov.*, 990
in respiratory allergy, technique, *Nov.*, 990
preparation of, *Nov.*, 990
for poliomyelitis, *May*, 500
Vaccine treatment in allergic respiratory conditions, value of, *Nov.*, **987–993**
Vaccinia infections, treatment with immune substances, *May*, 418
Valvulotomy, for pulmonary stenosis, *Feb.*, 201
for tetralogy of Fallot, *Feb.*, 207
punch, for infundibular stenosis, *Feb.*, 208
Vascular ring, *Feb.*, 183
Veins, pulmonary, anomalous entrance into right auricle, venae cavae or coronary sinus, diagnosis, *Feb.*, 144
partial anomalous connection, pathology, *Feb.*, 29
partial anomalous drainage, diagnosis, *Feb.*, 127
total anomalous connection, pathology, *Feb.*, 44
Vena cava, superior, left, persistent, anomalous connection with left atrium, pathology, *Feb.*, 48
Ventricle(s), common ejectile force for systemic and pulmonary circulations, pathology, *Feb.*, 33
left, failure of, pathology, *Feb.*, 14
Ventricle(s), left, hypertrophy of, electrocardiographic patterns, *Feb.*, 137
fluoroscopic and roentgenographic findings, *Feb.*, 136
increased work of, conditions causing, *Feb.*, 116
right, absent, with cyanosis, pathology, *Feb.*, 46
hypertrophy, electrocardiographic patterns, *Feb.*, 138
fluoroscopic and roentgenographic findings, *Feb.*, 135
increased work of, conditions causing, *Feb.*, 124
nonfunctioning, surgical treatment, *Feb.*, 207
single, angiocardiography in, *Feb.*, 84
with hypoplastic pulmonary artery, diagnosis, *Feb.*, 141
with normal-sized or dilated pulmonary artery, diagnosis, *Feb.*, 144
without pulmonary stenosis, surgical treatment, *Feb.*, 213
Ventricular septum, defect of, angiocardiography in, *Feb.*, 87
diagnosis, *Feb.*, 119
in muscular portion, diagnosis, *Feb.*, 127
pathology, *Feb.*, 14
intact, and atrial septal defect, with pulmonary valvular stenosis, pathology, *Feb.*, 33
with pulmonary valvular atresia, pathology, *Feb.*, 42
murmurs, *Feb.*, 10
Vitamin A, absorption, in allergic celiac syndrome, *Nov.*, 1011
for premature infant, *Aug.*, 582, 655, 671
Vitamin D for premature infant, *Aug.*, 582, 655, 671
Vitamin K for premature infant, *Aug.*, 672
Vitamin therapy for premature infants, *Aug.*, 645
Volvulus, in newborn, *May*, 310
treatment, *May*, 311
midgut, with malrotation, *Nov.*, 916
Vomiting, fluid therapy in, *Nov.*, 882
recurrent, as symptom of gastrointestinal allergy, *Nov.*, 998

Water, deficit of, and hyperosmolarity complicated by convulsions, *May*, 346
requirements, daily, of premature infants, table, *Aug.*, 655
Weight, gain, in pregnancy. See *Pregnancy.*
in celiac syndrome and mucoviscidosis, *May*, 396
Wilson phenomenon, *Feb.*, 52
Wolff-Parkinson-White syndrome, *Feb.*, 230

Your Child's Operation, *Aug.*, **721–742**